Anaphylaxis in a Central University Hospital - A two decade comparison study

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Anaphylaxis is the most severe clinical presentation of acute systemic allergic reactions [1]. Recent publications show an increasing time trend for hospitalizations due to anaphylaxis, especially in the paediatric population, accounting for up to 0.26% of overall admissions [2]. Lack of awareness around healthcare workers can lead to under diagnosis and under or delayed treatment of this medical emergency. In 2004, the first definition and criteria were proposed [3]. Since then, a number of papers have been published regarding the diagnosis, acute management, and prevention of anaphylaxis [1, 4, 5].

We performed a clinical record's review of hospitalized patients in a Portuguese University Hospital, between January 2007 and 2017 (2nd decade), with a diagnosis of anaphylaxis/anaphylactic shock. Results were compared with a previous study from January 1996 to 2006 (1st decade) [6].

A total of 69 clinical charts were reviewed in the 2nd decade, versus (vs) 72 in the 1st. Sixteen cases (23%) were excluded in the 2nd vs 19 (26%) in the 1st, resulting in a total of 53 patients for each decade. Considering hospital admissions of all causes, the rate of anaphylaxis was approximately 0.01% in both decades. The majority were female (57% vs 53%, 2nd vs 1st decade) with a mean age of 52±27.3 (vs 45±31.4), and 21% of the patients had self-reported allergic

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diseases vs 26% (table 1). Of the total number of admissions, 17% of patients were aged ≤ 18 years old vs 15%.

In contrast to the 1st decade, where 35 patients (66%) were admitted for anaphylaxis/anaphylactic shock, these diagnoses were less prevalent as a primary diagnosis in the 2nd decade, with 40 patients (75%) admitted for non–anaphylaxis causes. Drugs were the largest group of suspected trigger agents in both decades. When comparing culprit agent frequencies between the 2nd and 1st decades, respectively, we found that drugs were involved in 81% vs 85% of cases; food in 13% of cases in both decades; dyes and blood products in 2% vs 0% each; and hymenoptera venom (HV) in 2% of the cases in the 1st decade. One case (2%) was considered idiopathic, in the 2nd decade, in a patient with mastocytosis.

Regarding drugs, β-lactam antibiotics were most frequently implicated in the 2nd but not in the 1st decade, where contrast media were responsible for the majority of drug-related reactions. As for food, the main route of contact was ingestion, except for one reaction (1st decade), which occurred after a child entered a room where nuts were being cracked, citing “inhalation” as the only point of contact. All the implicated agents are listed in table 1.

Reactions mostly occurred within the 1st hour (75% vs 85%, 2nd vs 1st decade). Nearly 45% had ≥3 organ systems involvement vs 32% (2nd vs 1st decade, $p<0.01$). Cardiovascular symptoms were those most frequent (81%), followed by respiratory (75%) in the 2nd decade, in contrast to what was found in the 1st decade (43% respiratory and 39% cardiovascular symptoms, $p<0.01$ for both). Cutaneous were the third most frequent symptoms in both decades (72% vs 38%, 2nd vs 1st decade respectively, $p<0.01$), followed by gastrointestinal involvement (17% and 6%). Biphasic reaction occurred once (vs 0) and 4% had a cardiac arrest (vs 15%). Mortality rate decreased between both decades (4% vs 6%, $p>0.05$).

Of all the patients who died as a result of the anaphylactic reaction, the suspected agents were drugs in 4 cases (β-lactams, rifampicin, methylprednisolone/acetylsalicylic acid/paracetamol

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and contrast medium), and blood products (platelets) in one. Of the deceased patients, 40% had a prior history of a drug hypersensitivity, one involving the suspected agent (rifampicin); 40% were hospitalized for reasons other than anaphylaxis/anaphylactic shock.

Adrenaline was administered in 64% of the patients (vs 55%) and referral to the Allergy and Clinical.

Immunology (ACI) outpatient clinic occurred in 43% vs 23% (p=0.03 and p=0.02 respectively).

Considering that adrenaline auto injector (AAI) is not usually recommended in drug reactions, we analysed AAI prescription only in anaphylaxis to food, HV and idiopathic reactions. Five out of 8 patients had AAI prescription in the 2nd decade vs 1/8 in the 1st.

We tried to explore the evolution of the epidemiology, aetiology and management of anaphylaxis in two consecutive decades in the same hospital. An inversion of the primary/secondary diagnosis ratio was observed, decreasing considerably as a primary diagnosis from the 1st to the 2nd decade (0.008% to 0.003%, respectively). This could be explained by a predominantly adult population or that our emergency department patients can remain under surveillance for up to 24 hours, if required, without hospitalization. Only about 11% these emergency episodes result in hospitalization.

When comparing with studies performed in clinical settings, a predominance of drug-triggered reactions was likewise found [7,8]. Interestingly, a new group of drugs arose in the 2nd decade: chemotherapeutic drugs. In fact, in a Korean study, chemotherapies were the major causative agents of in-hospital anaphylaxis cases (42% of cases) [9]. In our hospital, the majority of reactions to chemotherapies occurs in a day care hospital setting, where patients are evaluated by allergists and rarely is hospitalization necessary. We also found an unexpectedly low frequency of mucocutaneous symptoms (less than 80%) in both decades. This could be attributed to a possible undervaluation/underreporting of said manifestations by health

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professionals, or due to resolution of these symptoms at hospital entry, spontaneously or related to prior treatment.

Additionally, an improvement in anaphylaxis management was observed, with an increase in adrenalin emergency administration and referral to the ACI outpatient clinic, although both remained below expectations, referral rate particularly as more than half of the patients continued to lack referral .As for AAI prescription, it increased almost five times between decades in food, HV and/or idiopathic cause, although is difficult to assess the significance due to the limited number of episodes.

Although progress was evident, Allergy and Clinical Immunology still play an important role in filling the gaps both in the recognition and management of anaphylaxis as in the evaluation and long –term follow-up of these patients.

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Conflicts of interest

None.

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Table 1. Suspected trigger agents.

		2nd Decade (n)	1st Decade (n)
Drugs		**44**	**49 / 85**
	β-lactam antibiotics	15	8
	Contrast media	9	10
	Non-β-lactam antibiotics	4	6
	NSAIDs	4	7
	Other analgesics	1	4
	Chemotherapy	3	0
	Others	8	14
Foods		**7**	**7**
	Nuts	2	3
	Cow's milk	2	0
	Seafood	2	1
	Fresh fruits	1	2
	Legumes	0	1
Blood products		**1**	**0**
Hymenoptera Venom		**0**	**1**

NSAIDs: non-steroidal anti-inflammatory drugs.

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