SPECIAL CONSIDERATIONS ON ANAPHYLAXIS IN LATIN AMERICA

Edgardo J Jares, MD
President-elect Sociedad Latinoamericana de Alergia Asma e Inmunología
ANAPHYLAXIS

- Severe life-threatening generalized or systemic hypersensitivity reaction

- Swelling of the conjunctiva
- Runny nose
- Swelling of lips, tongue and/or throat
- Heart and vasculature
  - fast or slow heart rate
  - low blood pressure
- Skin
  - hives
  - itchiness
  - flushing
- Central nervous system
  - lightheadedness
  - loss of consciousness
  - confusion
  - headache
  - anxiety
- Respiratory
  - shortness of breath
  - wheezes or stridor
  - hoarseness
  - pain with swallowing
  - cough
- Gastrointestinal
  - crampy abdominal pain
  - diarrhea
  - vomiting
  - Loss of bladder control

Circulatory collapse and complete airway blockage can be fatal

Epidemiology

- Incidence: 3 to 300 per 100 000 person years
- Lifetime prevalence: 0.05-2%

Gupta R et al, Thorax 2007
Hospital admissions from all-cause anaphylaxis increased by 615% over the time period studied, but annual fatality rates remained stable at 0.047 cases (95% CI, 0.042-0.052 cases) per 100,000 population.

Food-triggered anaphylaxis were most common in young people, with a marked peak in the incidence of fatal food reactions during the second and third decades of life.

Admission and fatality rates for drug- and insect sting–induced anaphylaxis were highest in the group aged 60 years and older.

First European Anaphylaxis Registry

- 10 European countries
- Online questionnaire
- Fifty-nine centers reported 3333 cases of anaphylaxis (2011-2014)
- Pilot study for European Registry

EUROPE: MAIN INDUCERS

Adults

- Insects: 48%
  - 79% from Germany (yellow jackets and bees)
- Foods: 20%
- Drugs: 23%
- Others: 9%

Children

- Insects: 20%
- Foods: 65%
- Drugs: 5%
- Others: 10%

34.2% previous, most frequently milder reaction to the same allergen


<table>
<thead>
<tr>
<th></th>
<th>Austria</th>
<th>Bulgaria</th>
<th>France</th>
<th>Germany</th>
<th>Greece</th>
<th>Ireland</th>
<th>Italy</th>
<th>Poland</th>
<th>Spain</th>
<th>Switzerland</th>
<th>All countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>First/Recurrent</td>
<td>91/29</td>
<td>22/8</td>
<td>194/81</td>
<td>882/371</td>
<td>11/5</td>
<td>6/4</td>
<td>18/25</td>
<td>18/16</td>
<td>89/30</td>
<td>154/61</td>
<td>1485/630</td>
</tr>
</tbody>
</table>

- **Adrenaline**
- **Antihistamines**
- **Beta-2-mimetics**
- **Corticosteroids**
- **Oxygen**
- **Volume**
ANAPHYLAXIS IN AMERICA

- Two nationwide, cross-sectional random-digit-dial surveys: patients and public
- Standardized questionnaires
- The public survey included 1,000 adults
  + 5.1 and 1.6% probable and very likely anaphylaxis.
- The patient survey included 1,059 respondents: subjects who reported experiencing some type of generalized allergic reaction: 32.5% history of anaphylaxis

Wood R et al. J ALLERGY CLIN IMMUNOL 2014
ANAPHYLAXIS IN AMERICA

Public Survey

Ever had an allergic reaction to:

- Drugs 34%
- Insects 20%
- Food 16%
- Latex 6%
- Others 23%

Patients Survey

- Drugs 32%
- Insects 21%
- Food 20%
- Latex 7%
- Others/idiopathic 20%

Wood R et al. J ALLERGY CLIN IMMUNOL 2014
Online Latin American Survey of Anaphylaxis (OLASA)
Developed by Latin American Society of Allergy, Asthma and Immunology
634 patients from 15 countries were registered
ANAPHYLAXIS IN LATIN AMERICA

Clinical manifestations

- Cutaneous: 94%
- Respiratory system: 79%
- Cardiovascular system: 40%
- Gastrointestinal system: 30.4%

Anaphylaxis online survey in Latin America
ANAPHYLAXIS IN LATIN AMERICA

Anaphylaxis online survey in Latin America
ANAPHYLAXIS IN LATIN AMERICA

Drugs: 31.2%
- NSAIDs: 22.7%
- Antibiotics: 5.6%
- Others: 1.9%
- Local Anesthetics: 0.8%

Food: 23.3%
- Fish/seafood: 10.7%
- Wheat: 2.9%
- Fruits: 3.2%
- Peanut: 1.4%
- Corn: 0.4%
- Nuts: 1.1%
- Manioc: 0.4%

Insects: 14.8%
- Bees: 7.4%
- Wasps: 2.8%
- Ants: 4.6%

Anaphylaxis online survey in Latin America
### Table 1: Main triggering agents for severe allergic reactions according to the age of patients registered in the Online Latin American Survey on Anaphylaxis.

<table>
<thead>
<tr>
<th>Agents</th>
<th>Age (years)</th>
<th>Total</th>
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<tbody>
<tr>
<td></td>
<td>&lt;2</td>
<td>2–5</td>
</tr>
<tr>
<td></td>
<td>31 (16.3%)</td>
<td>28 (14.7%)</td>
</tr>
<tr>
<td>Food – total</td>
<td>16 (53.3%)</td>
<td>16 (56.5%)</td>
</tr>
<tr>
<td>Cow’s milk</td>
<td>7 (22.6%)</td>
<td>7 (25.0%)</td>
</tr>
<tr>
<td>Egg</td>
<td>8 (25.8%)</td>
<td>5 (17.9%)</td>
</tr>
<tr>
<td>Fish/seaweed</td>
<td>–</td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>Peanuts</td>
<td>–</td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>Nuts</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Manioc</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Corn</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fruits</td>
<td>1 (3.2%)</td>
<td>2 (7.1%)</td>
</tr>
<tr>
<td>Wheat^</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Soy</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Insects – total</td>
<td>8 (26.7%)</td>
<td>11 (39.1%)</td>
</tr>
<tr>
<td>Bee</td>
<td>–</td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>Ants</td>
<td>7 (22.6%)</td>
<td>9 (32.1%)</td>
</tr>
<tr>
<td>Wasp</td>
<td>1 (3.2%)</td>
<td>1 (3.6%)</td>
</tr>
</tbody>
</table>

The most commonly involved sites were the skin, oropharynx, and upper respiratory tract.

Drugs: 98 episodes

- NSAIDs
  - selective 11%
  - cross 78%
- Oral Mites 8%
- Food 26%
- Exercise 2%
- Latex 2%
- Insects 4%
- β-Lactam 4%

Female 70.4% Children 6.7%
Anaphylaxis and Acute Allergic Reactions in ED between 2007-2009

- Six patients (4.4%) anaphylaxis
- 129 patients (95.6%) allergic reactions.
- Among the patients diagnosed with allergic reactions, 25 (23%) met the diagnostic criteria for anaphylaxis but were not recognized.

Calderon E et al. Anaphylaxis Diagnosis and Treatment at an Emergency Department in Puerto Rico. PRHSJ Vol. 32 No. 4 • December, 2013
Calderon E el al. *Anaphylaxis Diagnosis and Treatment at an Emergency Department in Puerto Rico.* PRHSJ Vol. 32 No. 4 • December, 2013
Table. Summary of Survey Results According to Physician Specialty (Allergy and Immunology) and Work in Emergency Care (EC)

<table>
<thead>
<tr>
<th></th>
<th>Allergy and Immunology Specialist</th>
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<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>EC(^a) n=51 (%)</td>
<td>Not EC(^b) n=299 (%)</td>
<td>Total(^c) n=350 (%)</td>
<td>EC(^a) n=77 (%)</td>
<td>Not EC(^b) n=83 (%)</td>
<td>Total(^c) n=160 (%)</td>
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</tr>
<tr>
<td><strong>Which laboratory test supports the clinical diagnosis of anaphylaxis?</strong></td>
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<tr>
<td>Total serum tryptase</td>
<td>41 (80.4)</td>
<td>213 (71.2)</td>
<td>254 (72.6)</td>
<td>14 (18.2)</td>
<td>14 (16.9)</td>
<td>28 (17.5)</td>
<td>a&gt;b; c&gt;f; a&gt;d; d&gt;e</td>
<td></td>
</tr>
<tr>
<td><strong>What is the treatment of choice for anaphylaxis?</strong></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM epinephrine</td>
<td>40 (78.4)</td>
<td>209 (69.9)</td>
<td>249 (71.1)</td>
<td>20 (26.0)</td>
<td>18 (21.7)</td>
<td>38 (23.8)</td>
<td>d&gt;e; c&gt;f; a&gt;d; c&lt;f; a&lt;d; b&lt;e</td>
<td></td>
</tr>
<tr>
<td>SC epinephrine</td>
<td>6 (11.7)</td>
<td>64 (21.4)</td>
<td>70 (20.0)</td>
<td>38 (49.4)</td>
<td>36 (43.4)</td>
<td>74 (46.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>When should epinephrine be administered in anaphylaxis?</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient in shock</td>
<td>7 (13.7)</td>
<td>36 (12.0)</td>
<td>43 (12.3)</td>
<td>26 (33.8)</td>
<td>23 (27.7)</td>
<td>49 (30.6)</td>
<td>c&lt;f; a&lt;d; b&lt;e</td>
<td></td>
</tr>
<tr>
<td>When anaphylaxis is suspected</td>
<td>44 (86.3)</td>
<td>263 (88.0)</td>
<td>307 (87.7)</td>
<td>51 (66.2)</td>
<td>60 (72.3)</td>
<td>111 (69.4)</td>
<td>c&gt;f; a&gt;d; b&gt;e</td>
<td></td>
</tr>
</tbody>
</table>

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS ARE MAJOR CAUSES OF DRUG-INDUCED ANAPHYLAXIS

Seventy-eight patients (66.7%) reported previous reactions to the drug involved in the current reaction or to a drug from the same class and/or group.

Nonsteroidal anti-inflammatory drugs are major causes of drug-induced anaphylaxis

- Epinephrine use: 34%, and less than 50% of patients with cardiovascular involvement

 Patients presenting anaphylaxis were selected in a descriptive cross-sectional study using ENDA questionnaire

 Implemented in 22 allergy units from 11 Latin American countries

 U/A+ R-GI and/or CV Symptoms

 Or 2 of the following symptoms:
  + Respiratory, persistent GI or CV symptoms

 From 1005 HDR, 264 presented anaphylaxis

 Jares E et al, JACI in practice 2015
DRUG-INDUCED ANAPHYLAXIS IN LATIN AMERICA
STRIKING FINDINGS

- Severe reactions were present in 43% of atopic patients and 59% of non-atopic patients (p<0.01)
- Asthma patients have less severe reactions (38.6%) than non-asthmatic patients (54.6%) (p<0.05)

Jares E et al, JACI in practice 2015
**Asthma, Allergy and Anaphylaxis**

- González Pérez et al (UK) found a 2 fold and 3.3 fold greater risk of anaphylaxis in non-severe and severe asthmatics respectively.

- Greenberger PA and Simmons FE:
  - Severe and uncontrolled asthma → risk factor for more severe anaphylaxis

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Gonzalez Pérez et al. J Allergy Clin Immunol 2010;125:1098-1104
Simmons FE, J Allergy Clin Immunol 2009
716 patients with an ED visit and/or hospitalization for DIA

Patients with DIA and atopy or asthma did not differ with respect to severity, site of treatment or management compared with patients without any concomitant allergic condition

Aun M, and Faria E presented similar findings

Park H et al did not find difference in atopy/asthma in anaphylaxis with or without shock

The presumption that atopic predisposition contributes to a more severe allergic reaction to drugs, as stated in many publications, requires further investigation.
DRUG INDUCED ANAPHYLAXIS IN LATIN AMERICA

- U/A y R-GI: most frequent symptoms
- More than 45%: CV involvement

CV symptoms were more frequent in elderly patients (85%) than in adults (45.7%) and children (30.6%; p<0.00001)

Jares E et al, JACI in practice 2015
In our study, shock and severe anaphylaxis were more frequent in elderly patients.

- In an Australian study of death in anaphylaxis, most drug-induced anaphylaxis deaths occurred between 55 and 85 years old patients.

IN OUR STUDY, SHOCK AND SEVERE ANAPHYLAXIS WERE MORE FREQUENT IN ELDERLY PATIENTS

- Park et al found that elderly patients with anaphylaxis were at increased risk for the development of shock.

More than 15% of the patients had suffered a previous DHR with the same drug.

Jares E et al, JACI in practice 2015
ANAPHYLAXIS INDUCERS

**NSAIDS PREDOMINANCE**

- **Latin-America**

- **Other regions**
  - Çelik GE, Allergol Immunopathol (Madr). 2013. (Turkey)

**BETA LACTAMS PREDOMINANCE**

**DRUG INDUCED ANAPHYLAXIS IN LATIN AMERICA**

<table>
<thead>
<tr>
<th>NSAIDs</th>
<th>Selective Reactivity 1/3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipyren</td>
<td>25% (Renauldin et al)</td>
</tr>
<tr>
<td>ASA</td>
<td>20%</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>15%</td>
</tr>
<tr>
<td>Didofenac</td>
<td>10%</td>
</tr>
<tr>
<td>Acetamindophen</td>
<td>5%</td>
</tr>
<tr>
<td>Naproxen</td>
<td>1%</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>1%</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>1%</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>1%</td>
</tr>
<tr>
<td>Difunisal</td>
<td>1%</td>
</tr>
<tr>
<td>Nimesulide</td>
<td>1%</td>
</tr>
</tbody>
</table>

*Pyrazolone compounds: 1° cause, similar to Brazil (Aun et al), different to Portugal (Faria et al) and Spain (Quiralte et al)*

Faria E et al, J Investig Allergol Clin Immunol 2014
Renauldin et al, Allergy 2013

Jares E et al, JACI in practice 2015
TREATMENT: 78% WERE TREATED IN THE EMERGENCY DEPARTMENT, AND 8.7% HOSPITALIZED

Only 27% of anaphylaxis patients recieved epinephrine, 39.2% when CV symptoms were present

Jares E et al, JACI in practice 2015
EPINEPHRINE USE

- The low epinephrine use in anaphylaxis treatment is common in studies from Latin America and other regions.
Banerji et al: only 8% of patients with drug-induced anaphylaxis treated in the ED received epinephrine

CONCLUSIONS

- The relationship between atopic predisposition/asthma and anaphylaxis requires further investigation
- NSAIDs are the most frequent anaphylaxis inducers in Latin-America
- Epinephrine is underuse in anaphylaxis treatment in Latin America and other regions
- Medical education of ED physicians in Latin America should focus on this topic