Title: Drug induced Anaphylactic reactions in Indian population: A systematic review

Review question(s)
To carry out a systematic review of the published evidence of the drug induced anaphylactic reactions in Indian population

Searches
1. Sources for search include:
   (i) Electronic databases: PubMed, PUBMED Central, Google Scholar, Cochrane
   (iii) Bibliographies of relevant articles.
   (iii) Indian journals publishing the articles in the field of medicine, critical care, emergency medicine, dermatology, pharmacology and adverse drug reactions available on internet

2. Time period to be considered by the review: From 1998 to 2013

3. Language restrictions: Articles in English language only will be included

4. The search strategy will include the following key search terms: ‘anaphylactic reaction’ OR ‘immediate reaction’ OR ‘anaphylactic shock’ AND (‘India’ OR ‘Indian population’).

<table>
<thead>
<tr>
<th>Search Strategy for Pubmed</th>
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<tbody>
<tr>
<td>1. Anaphylactic reaction</td>
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<td>2. Immediate reaction</td>
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<td>3. Anaphylactic shock</td>
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<td>4. or/1-3 AND India</td>
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<tr>
<td>5. or/1-3 AND Indian Population</td>
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Types of study to be included
1. Observational studies (cohort, case-control, case series, case reports)

Condition or domain being studied
The anaphylaxis is a rare potentially life threatening form of hypersensitivity reactions that occurs suddenly after contact with an allergen. The binding of allergen to Ig E on mast cells and basophiles releases inflammatory immune mediators which increases vascular permeability, peripheral vasodilatation and bronchial smooth muscle contraction. It can affect any organ in the body but cutaneous, respiratory, cardiovascular, gastrointestinal and neurology are the commonly affected systems. Any agent capable of stimulating mast cells or basophiles can cause anaphylaxis. The common offenders for anaphylaxis are drugs, food, insect bites, venom, intravenous contrast materials, and latex. The common drugs causing anaphylaxis are anaesthetic medications, antibiotics, NSAIDs. However, there are no testing methods or known risk factors available to differentiate individuals at risk for anaphylactic reaction from a simple allergic reaction. Exception to this is the individuals with asthma who may suffer a more severe reaction.
Most of the epidemiological data on anaphylaxis are based on studies on developed countries. The data regarding its causative agents, clinical pattern, incidence, risk factor, management and outcome are limited from the developing and low income countries.

**Participants/ population**

**Inclusion:**
- Studies on Indian population only
- All Prospective or retrospective studies related to anaphylactic reactions
- All cohort, case-control, case series, case reports, letter to editors related to drug induced anaphylactic reactions
- Studies related to adverse drug reactions that have described the anaphylactic reactions
- All age groups and clinical settings (Indoor or outdoor patients)

**Exclusion:**
- Studies which is not based on Indian population
- All cohort, case-control, case series, case reports, letter to editors related to other etiologies of anaphylactic reactions (e.g., food, insects, parasitic diseases, etc.)
- Editorials, review articles, non-research letters and discussion papers
- Animal studies

**Intervention(s), exposure(s)**
- No intervention and exposure

**Comparator(s)/ control**
Data from this study will be compared with the similar studies performed on other than Indian Population

**Context**
1. By study settings: All types of setting- outdoor and indoor
2. By case definition: this will be based on clinical case criteria defined by Sampson HA et al, J Allergy Clin Immunol 2006;117:391–397.

**Outcome(s)**

**Primary outcome**
1. Causative drugs for anaphylactic reactions in Indian population
   a. Causative drugs will include herbal drugs, anaesthetic agents and vaccines.

**Secondary outcomes**
1. Frequency distribution of age, gender, setting of cases
2. Risk factors for the drug induced anaphylactic reactions
3. Difference in clinical presentation -
   a. between adult and paediatric patients
   b. between patient with and without allergic diseases
4. lag period (time for the onset of anaphylaxis from exposure to causative agents)
5. Duration of hospital stay
6. Therapy administered at initial anaphylaxis
7. Outcome of reaction
8. Preventability assessment: percentage of preventable reactions with reasons of preventability
9. Causality assessment
10. Severity assessment

Data extraction, (selection and coding)
The two reviewers will independently extract data from the included studies and case report. Any disagreements will be discussed and resolved by a consensus.

Risk of bias (quality) assessment
The ‘STROBE statement’ will be used to assess the quality of reporting of the cohort, case-control and case-series studies. The ‘CARE guideline’ will be used to assess the quality of reporting of the case reports. The risk of bias and quality of individual study will be evaluated by appropriate risk assessment tools at both the study and outcome level.

Strategy for data synthesis
a) Data will be extracted and summarized using central tendency measures (ranges, medians or means) and the proportions as provided by the authors.
b) Missing data: ‘A worse case’ scenario will be used in case of missing outcome data. The sensitivity analyses will be performed to test the robustness of imputations.
c) Statistical package: Graph Pad Prism version 5.0

Subgroup analysis

Statistical analysis

Dissemination plans
Abstract will be submitted for presentation at an appropriate conference. Manuscript will be submitted for publication to a peer-reviewed journal.

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None

**Conflicts of interest**
None

**Language**
English

**Country**
India

**Subject index terms**
Anaphylactic reactions

**Date of registration in PROSPERO :**

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<th>Stage of review at time of this submission</th>
<th>Started</th>
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<tr>
<td>Preliminary searches</td>
<td>Yes</td>
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<td>Piloting of the study selection process</td>
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<tr>
<td>Formal screening of search results against eligibility criteria</td>
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<td>Data extraction</td>
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