Refractory anaphylaxis: Data from the European Anaphylaxis Registry

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Text of abstract

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# Abstract:

Refractory anaphylaxis (unresponsive to treatment with at least 2 doses of minimum 300 mg adrenaline) is a rare and often fatal hypersensitivity reaction. Based on this, definition, its prevalence, and risk factors are only vaguely described.  
Using the data from the European Anaphylaxis Registry (11596 cases in total) we were able to identify cases of refractory anaphylaxis (n = 42) and to analyse these in comparison to a control group of severe anaphylaxis cases (n = 4820). The data show that drugs more frequently elicited refractory anaphylaxis (50% of cases, p < 0.0001) than in other severe anaphylaxis cases (18.4%). Cases elicited by insects (n = 8) were more often due to bees in refractory cases (62.5% vs 19.4%, p = 0.00921). The refractory cases occurred more frequently in a perioperative setting (45.2% vs. 9.05, p < 0.0001). Intramuscular adrenaline (as a first line therapy) was administered in 17.5% of refractory cases, whereas in 87.5% of cases was given intravenously (significantly more often than in severe anaphylaxis cases: 14.1%, p < 0.0001). Second line treatment options (e.g. vasopression with dopamine, methylene blue, glucagon) were not used at all in the treatment of refractory cases. The mortality rate in refractory anaphylaxis was significantly higher (26.2%) than in severe cases (0.353%, p < 0.0001). Although multiple guidelines on anaphylaxis have been published, the clinical adherence to these standards can be improved. The low use of intramuscular adrenaline as a first line therapy might contribute to refractoriness of an episode. Also, the lack of suggested second line medication use in refractory cases indicate that the availability of these drug is restricted or anaphylaxis management guidelines may need a revision in order to provide clear algorithms for severe refractory anaphylaxis.

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# References

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# Figures

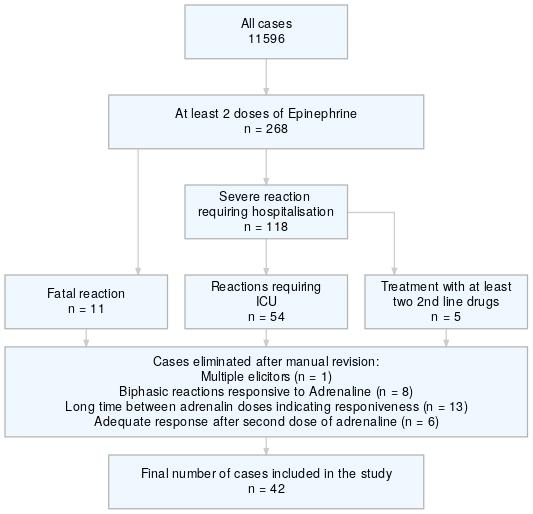


Figure 1 Flowchart illustrating the cases selection process for the final database.

# Tables

Table 1 Summary of the refractory anaphylaxis cases.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | n | Age | Cardiologic | DM | Food allergy |
| female | 22 | 40 | 31.8 | 9.09 | 13.6 |
| male | 20 | 43 | 30 | 15 | 5 |

Table 2 Summary of elicitors in the refractory anaphylaxis cases and severe anaphylaxis cases as a control.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | n | refractory ANA [%] | severe ANA [%] | p value | Age | Male sex [%] | Perioperative [%] | Food allergy [%] |
| food | 9 | 21.4 | 33.5 | 0.856 | 17.4 | 55.6 | 0 | 33.3 |
| drugs | 21 | 50 | 18.4 | 1.2e-05 | 48.8 | 42.9 | 90.5 | 0 |
| insects | 8 | 19 | 38.7 | 0.00014 | 46.5 | 62.5 | 0 | 0 |
| other | 2 | 4.76 | 3.38 | 0.361 | 38 | 0 | 0 | 50 |
| unkown | 2 | 4.76 | 6.02 | 1.2e-05 | 55.5 | 50 | 0 | 0 |

Table 3 Summary of elicitors in the refractory anaphylaxis cases and severe anaphylaxis cases as a control.

|  |  |  |  |
| --- | --- | --- | --- |
| Elicitor | severe ANA [%] | refractory ANA [%] | p value |
| antibiotics | 30.8 | 38.1 | 0.479 |
| xray\_cm | 4.78 | 14.3 | 0.0823 |
| legumes | 16.6 | 33.3 | 0.178 |
| bee | 19.4 | 62.5 | 0.00921 |
| yellow jacket | 69.3 | 25 | 0.013 |

* p-value derived from the Fischer exact test.

Table 4 Summary of therapeutic measures in the refractory anaphylaxis cases and severe anaphylaxis cases as a control.

|  |  |  |  |
| --- | --- | --- | --- |
| Therapy | severe ANA [%] | refractory ANA [%] | p value |
| q\_522\_adren\_im | 9.59 | 17.5 | 0.102 |
| q\_522\_adren\_iv | 14.1 | 87.5 | 1.25e-24 |
| q\_552\_adren\_iv\_v5 | 3.23 | 58.6 | 5.21e-17 |
| q\_522\_volume | 23.5 | 65 | 3.43e-08 |
| q\_552\_volume\_v5 | 14.9 | 27.6 | 0.0678 |
| q\_522\_antih\_iv | 46.8 | 67.5 | 0.0105 |
| q\_552\_antih\_iv\_v5 | 17.1 | 31 | 0.077 |
| q\_521\_cortic\_v5 | 33 | 37.5 | 0.724 |
| q\_522\_cortico\_iv | 55.8 | 77.5 | 0.00607 |
| q\_552\_cortico\_iv\_v5 | 23.9 | 41.4 | 0.0456 |
| q\_522\_beta2\_iv | 0.76 | 2.5 | 0.269 |
| q\_552\_beta2\_inhal\_v5 | 3.32 | 10.3 | 0.0776 |
| q\_522\_theo\_iv | 0.475 | 0 | 1 |
| q\_522\_o2 | 10.8 | 50 | 9.82e-10 |
| q\_552\_dopamine\_v5 | 0.185 | 0 | 1 |
| q\_552\_glucagon\_v5 | 0.0923 | 0 | 1 |
| q\_552\_methyleneb\_v5 | 0 | 0 | 1 |
| q\_561\_hospital\_admission\_v6 | 52.2 | 92.3 | 1.14e-07 |
| q\_562\_intensive\_care\_v6 | 14.1 | 84.6 | 3.72e-22 |

* p-value derived from the Fischer exact test.