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. Its definition, 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 compare them to a control group of severe anaphylaxis cases (n = 4820). Drugs significantly more frequently elicited refractory anaphylaxis (50% of cases) 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: vasopression with dopamine, methylene blue, glucagon i.v. were not used at all in the treatment of refractory cases. 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 leaves room for improvement. Low use of intramuscular adrenaline as a first line therapy might contribute to refractoriness of an episode. Also, lack of suggested 2nd line medication use in refractory cases indicate that availability of these drug is restricted or anaphylaxis management guidelines may need revision in order to provide algorithms for severe refractory anaphylaxis.

# Introduction:

The mainstay of Anaphylaxis management is the intramuscular dose of adrenaline, but in the most severe cases of anaphylaxis it might insufficient to restore a stable patient status.

Refractory anaphylaxis (although the established definition is lacking) might be defined as anaphylaxis meeting the criteria by NIAID/FAAN (**???**) which is unresponsive to the treatment with at least 2 doses of minimum 300 mg adrenaline (lack of expected normalization of clinical symptoms).

# Methods

We aimed to distinguish the prevalence of refractory anaphylaxis among anaphylaxis cases and factors which may increase the risk of a refractory anaphylaxis episode. Using the Data from the European Anaphylaxis Registry we selected cases where patients received at least two doses of adrenalin, and failed to recover adequately. The flowchart represents the detailed cases selection process.

The final database consisted of 42 cases from 7 countries: Germany: 19, Austria: 2, Switzerland: 11, Poland: 2, Spain: 1, France: 6, Ireland: 1.

# Results

The European Anaphylaxis Registry contained 11596 cases of anaphylaxis and in 268 cases at lest 2 doses of adrenalin were administered to the patient.

# Discussion

# Conclusion

# Acknowledgements

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# References

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# Figures

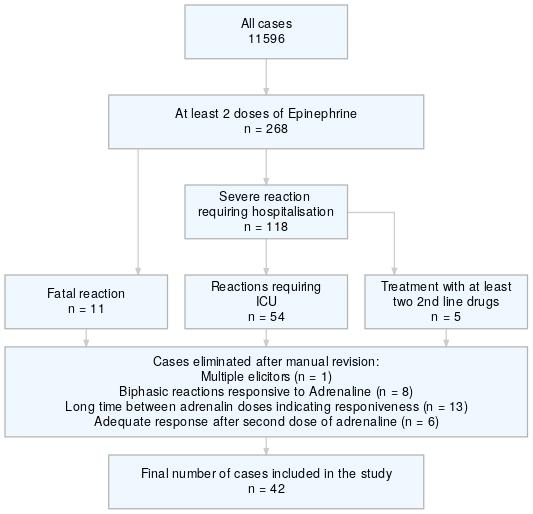


Figure 1 Flowchart illustrating the cases selection process for the final database.

# 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.