Refractory anaphylaxis: Data from the European Anaphylaxis Registry

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Abstract

Text of abstract

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1 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

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

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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2 References

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3 Figures

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- p-value derived from the Fischer exact test.
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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

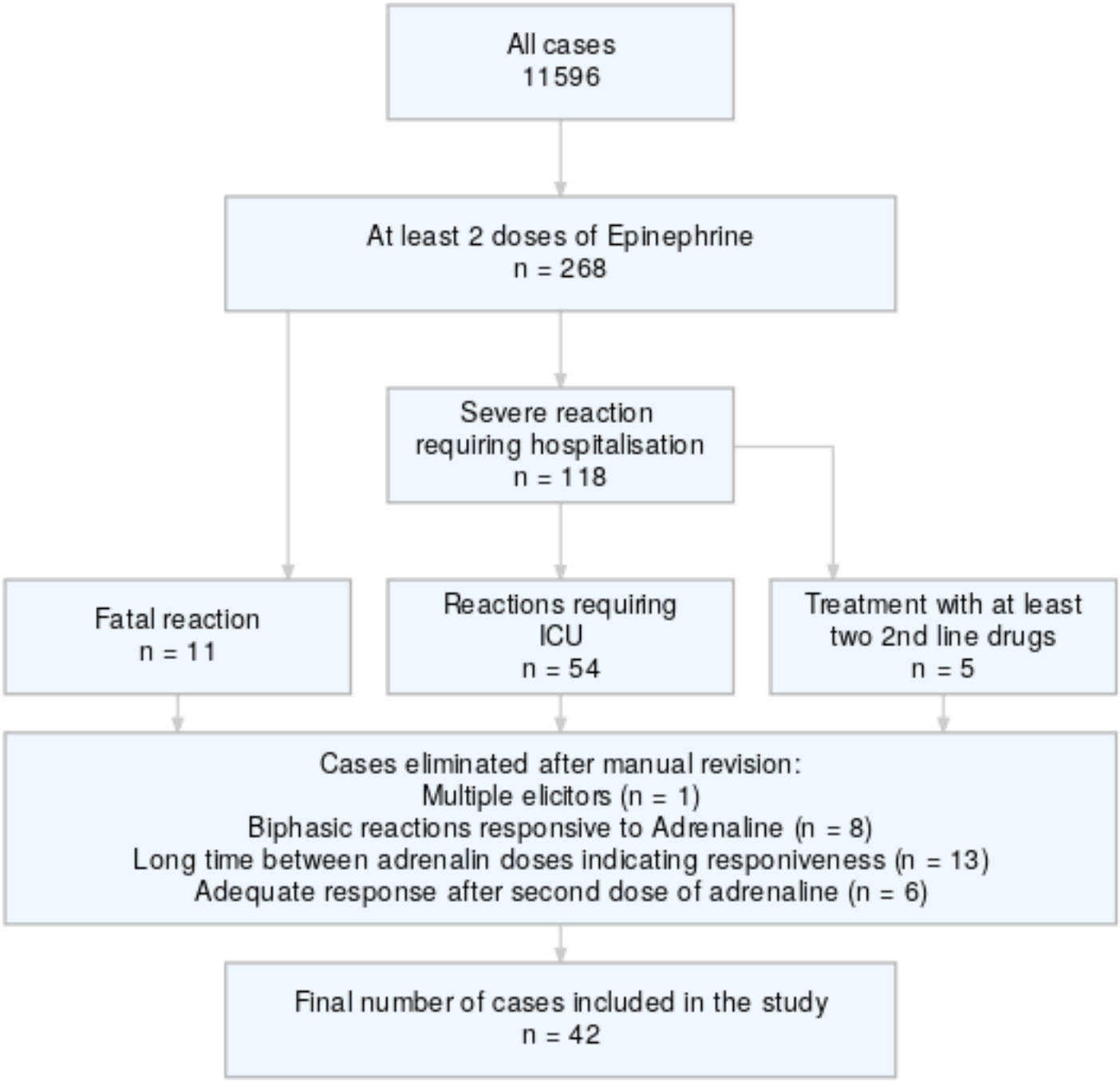

Figure 1: Flowchart illustrating the cases selection process for the final database.

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