

PREOPERATIVE ANAESTHESIOLOGIC EVALUATION OF PATIENT WITH KNOWN ALLERGY

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SUMMARY

Anaphylaxis is an unanticipated systemic hypersensitivity reaction which can produce deleterious effects, even death, if not treated promptly. Preventive approach implies taking a thorough anamnesis with the emphasis on previously diagnosed allergies. If an allergic reaction occurred during previous surgery, a detailed documentation of administered anaesthetic agents and drugs would be crucial for the following anaesthesiologic management. Preoperative planning and avoiding cross-reactivity with drugs commonly used during anaesthesia are the key points to prevent an anaphylaxis. In case of emergency surgery when the exact identification of allergens is not possible, premedication prophylaxis should be considered. General measures for prevention of anaphylaxis could be undertaken as well, such as the choice of anaesthesiologic drugs and techniques in the operating theatre adequately equipped for the management of predictable anaphylaxis.

Key words: anaesthesia - anaphylaxis - preoperative care

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Introduction

Anaphylaxis is an unanticipated systemic hypersensitivity reaction of an organism against a specific substance, which can produce deleterious effects, even death, if not treated promptly. Therefore, it is of immense importance for the attending physician always to be knowledgeable and vigilant of such potential adverse reactions.

All drugs and substances used during the conduct of anaesthesia, as well as during the surgery, may potentially cause anaphylaxis. Constant anticipation, and prevention of adverse events is the best strategy to help avoid anaphylaxis, or at least attenuate the severity of its sequels (Butterworth et al. 2013, Kroigaard et al. 2007).

Preventive approach should always be maintained, and it begins with a thorough anamnesis. Patient should be asked to report on any previously diagnosed allergies as well as on any other hypersensitivity reaction hitherto. Also, information on previous experience with anaesthesia, if applicable, or any other medical procedure may help shed light on possible triggers of hypersensitivity (De Hert et al. 2011).

Anamnesis and important questions about allergy

Preoperative anaesthesiologic evaluation of a patient with known allergic diathesis requires, as previously mentioned, a detailed anamnesis regarding hypersensitivity reactions, defining risk factors for anaphylaxis during the anaesthesia and detecting potential allergic cross-reactivity reactions between drugs, or food and

drugs, which then guides thorough preparation in the operating theatre. Anaphylaxis to anaesthetic agents is of foremost consideration, therefore, if any unexplained life-threatening reaction occurred during previous procedures involving anaesthesia, an allergic reaction should be suspected (Dewachter et al. 2011, Fisher 2007).

Investigation on allergic diathesis history usually starts with the question: "Have you ever had any allergic reaction to a specific drug/medicine or any other substance?" Many patients will report diarrhoea after taking some antibiotics, or stomach-ache after taking non-steroid antirheumatics – these are not allergic reactions. Conversely, some patients may not consider mentioning contact dermatitis or itching from wearing rubber gloves as relevant, but this information could indicate undiagnosed latex allergy, which can result in anaphylaxis during medical procedure. The patient should be informed that there is a potential danger of anaphylaxis during manual contact exposure, as all medical personnel are required to wear gloves to protect the patient and themselves. Therefore, questioning must be precise and succinct: "Have you ever experienced itching of the skin, eyes, nose or throat, rash or swelling of any part of the body after contact with, or ingestion, of food or drugs (antibiotics, latex, disinfecting agents)?" (Garvey 2011, Levy & Ledford 2017).

To detect underlying allergic diathesis, it is crucial to get the information on clinical features of the allergic reaction (Mertes et al. 2009). It is important to differentiate between reactions such as light rash against a severe reaction that includes difficulty with breathing, prolonged exhales, low blood pressure and urticaria. It

is also important to investigate if a medical intervention was required to alleviate the condition, such as adrenaline or antihistamines administration, as well as whether the condition required cardiopulmonary resuscitation, and/or hospitalization. Time frame between drug administration and clinical features development is also very important when considering allergic reaction manifestation – it can point out to a reaction mechanism (Pichler 2015). For example, latex allergy reaction usually occurs with more than one-hour delay (Harper et al. 2009).

Time passed since allergic reaction event is also to be considered – if the reaction occurred 10 years ago, the level of antibodies could have decreased subsequently, so the hypersensitivity reaction to repeated exposure to the substance in question might not even appear (Blumenthal & Solensky 2017). Ideally, anaphylaxis should be confirmed with tests, and the results documented and readily available to both the patient and to the attending physician (Garvey 2011). In practice this means that immediately after stabilization of the patient who had anaphylaxis, a serum tryptase should be done (Mertes et al. 2009); then in 4 to 6 weeks, patients should further undergo skin tests to determine the offending substance (neuro-muscular blockers, antibiotics, contrasts, barbiturates, etc.) (Scolaro et al. 2017).

Documentation – allergy reports

Ideally, if an allergic reaction occurred during previous medical procedure, a detailed documentation containing all relevant information regarding the reaction, procedure (anaesthesia/surgery/other medical) and drugs given, including follow up precautionary advisement, would be an invaluable asset to the anaesthesiologist in perioperative management of the patient (Gonzalez-Urbe et al. 2016).

Furthermore, this document should state all other drugs that had been administered to the patient simultaneously, or right before the incriminated substance. It is always possible that the concomitant drug triggered, or that it precipitated the allergic reaction. That way the list of suspected substances expands, but it should possibly help avoid subsequent re-exposure and anaphylaxis. At present, this kind of clinical practice remains rare. However, this should not discourage documenting allergic reactions (as well as any other medically adverse event), rather it should start to become routine to inform both the patient and their general practitioner of noted events in written (Krøigaard et al. 2005, Krøigaard et al. 2007).

Evaluation of risk factors for anaphylaxis

Risk factors for developing anaphylaxis during anaesthesia are previously documented allergy, information on possible allergic reaction during previous anaesthetic/surgical/other medical procedure, atopy (asthma,

allergic rhinitis, etc.) and medical history referring to hypersensitivity reactions to latex, which is very frequent in children who underwent repeated surgical procedures (e.g. correction of spina bifida, bladder exstrophy, etc.) and in adults who developed allergy to fruits, such as avocado, kiwi and bananas. Regarding age, allergic reactions are more frequent in women in their 40s and men in their 50s. Furthermore, women are 2-3 times more prone to develop anaphylaxis during anaesthesia (Fisher 2007, Gonzalez-Urbe et al. 2016, Hepner & Castells 2003, Manfredi et al. 2013, Liccardi et al. 2008, Michalska-Krzanowska 2012).

Preoperative planning and avoiding cross-reactivity with drugs commonly used during anaesthesia

Planning the anaesthetic procedure implies avoiding the use of substances suspected to most likely cause specific allergic reaction(s), thus identifying the right causative drug would be the safest approach to anaesthesia. Had the patient experienced anaphylaxis during previous anaesthesia/surgery/other medical procedure, one should undergo skin tests for the most common allergens (neuro-muscular blocking agents, antibiotics, latex, hypnotics) before an elective anaesthesia (Blumenthal & Solensky 2017, Ledford 2017, Mills et al. 2014).

Every substance used in perioperative period may cause allergic reaction (Hepner & Castells 2003, Garvey 2011). Of all drugs used in anaesthesia, neuro-muscular blocking agents (NMBAs) are the most incriminated substances that cause IgE-mediated anaphylaxis – in the descending order of importance these are: suxamethonium, rocuronium, vecuronium, pancuronium, mivacurium, atracurium and cisatracurium (Mertes et al. 2003). The cross-reactivity between NMBAs is common in approximately 60-70% of cases. It has been shown that pholcodine exposure raises IgE antibodies against NMBAs (as well as against pholcodine itself) and morphine (Harboe et al. 2007). Recent literature also implies cross reactivity with environmental factors (shampoos, detergents, toothpastes), which are yet to be determined (Harper et al. 2009).

Other drugs with higher allergenic potential than average including antibiotics, medical contrast dyes, chlorhexidine and, recently, a growing number of non-steroid anti-inflammatory agents have been reported, too.

Most commonly reported antibiotic in the world that causes allergic reaction is penicillin. However, since connection with anaphylaxis is mostly reported by patients themselves, who seldom have had any specific tests done, and yet for most of them the “allergic reaction” had been mild at worst (abdominal discomfort, rash), the data on incidence of allergy to penicillin is very unreliable. Although, a high level of suspicion is mandatory, and presents a mainstay of vigilant approach to avoiding anaphylaxis (Hepner & Castells 2003).

In patients allergic to penicillin, cephalosporines should be considered instead, during preoperative planning. Regarding cross-reactivity between penicillin and cephalosporin, it is attributed to the first generation cephalosporines while the cross-reactivity with the second and the third generation approaches 0%.

It is important to find out if the patient allergic to penicillin has ever taken cephalosporines – if there was no reaction to cephalosporines before, it makes perioperative use of cephalosporines preferable to vancomycin or carbapenems (Blumenthal & Solensky 2017).

Hypnotics generally have low allergenic potential. Hypersensitivity to barbiturates is most commonly reported, but in this situation non-barbiturates can be administered safely, while there is no cross-reactivity between barbiturates and non-barbiturates, as well as between non-barbiturates themselves. Therefore, non-barbiturates can be used even in case of documented allergy to barbiturates (Hepner & Castells 2003, Ledford 2017).

Propofol contains soybean oil and egg lecithin as emulsifying agents, however there is no contraindication for the use of propofol if patients refer allergy to eggs, soybean or peanuts – the lecithin in propofol is highly purified and allergenic proteins are cleaved from soy oil in the refinement process (Cochico 2012, Harper 2016).

Allergic reactions to etomidate and ketamine remain extremely rare (Mertes et al. 2009).

Benzodiazepines are also extremely safe drugs, although diazepam is reported to be more likely to cause allergic reaction than midazolam. On the other hand, anaphylactoid reactions to midazolam have been reported (Gonzalez-Urbe et al. 2016).

The incidence of allergic reactions to opioids is low, however sensitization to morphine can be caused by previous use of pholcodine. In case of an allergy to one of the opioids, another opioid may be used – fentanyl is usually an optimal choice, as it does not trigger direct mastocyte and basophil stimulation (Florvaag et al. 2005, Mali 2012).

Plasma volume expanders and blood products are also worth considering preoperatively as potential allergenic agents and alternative should be available in advance (Butterworth et al. 2013, Hirayama 2013, Varrier & Ostermann 2015).

In cardiac and vascular surgery settings, anaphylaxis on protamine-sulphate, although rare, does occur and should be anticipated in patients with insulin-dependent diabetes mellitus (patients taking NPH insulin), fish allergy, post-vasectomy and prior exposure to protamine-sulphate (Levy & Adkinson 2008).

Also, one must always keep in mind natural rubber latex, povidone-iodine and chlorhexidine use in perioperative setting (Dewachter et al. 2011, Mali 2012, Malsy et al. 2015).

Premedication prophylaxis

In case the exact identification of allergen(s) is not possible (e.g. emergency surgery), all drugs which had been administered to the patient before developing anaphylaxis should be avoided (of course, if such information is provided) and premedication with antihistamines and corticosteroids should be considered (Harper et al. 2009).

Different premedication protocols for patients at elevated risk for anaphylaxis can be found in literature (Liccardi et al. 2008). Combinations of anti-H1, anti-H2 and glucocorticoids are mostly used, with variability in time schedule (mostly depending on the level of urgency) and route of administration (Lasser et al. 1994). Most standardized protocols (Table 1) are the ones found in radiology suites regarding premedication prophylaxis for patients with previous acute reaction to iodinated intravenous contrast (Davenport et al. 2017). However, it is important to emphasize that the best prevention is to avoid the offensive substance – no pharmacologic prophylaxis guarantees full suppression of anaphylaxis, nor attenuation of it at the very least (Liccardi et al. 2008).

Table 1. Premedication prophylaxis for patients with iodinated contrast allergy

Non-urgent oral premedication
Glucocorticoid-preferred regimen: <i>Adult:</i> oral prednisone 50 mg at 13, 7 and 1 hour prior to contrast administration <i>Paediatric:</i> oral prednisone 0.5-0.7 mg/kg (max. 50 mg per dose) at 13, 7 and 1 hour prior to contrast administration
Glucocorticoid-alternate: <i>Adult:</i> methylprednisolone 32 mg iv. at 12 and 2 hours prior to contrast administration <i>Paediatric:</i> methylprednisolone 1 mg/kg iv. (max. 32 mg per dose) at 12 and 2 hours prior to contrast administration
And
H1 antihistamine: <i>Adult:</i> diphenhydramine 50 mg oral/ im./iv. 1 hour prior to contrast administration <i>Paediatric:</i> diphenhydramine 1.25 mg/kg oral/im./iv. (max. 50 mg) 1 hour prior to contrast administration

General measures for prevention of anaphylaxis

Other than avoiding the specific allergen and administering pharmacologic prophylaxis to patients, there are some general measures which could help alleviate the sequels of anaphylaxis. For example, patients with asthma should have respiratory symptoms under control as much as possible prior to undergoing anaesthesia, with continuous supervision, as they are prone to perioperative bronchospasm (Manfredi et al. 2013, Woods & Sladen 2009). Patients taking β -blockers are a

vulnerable group because β -blockers can increase the severity of anaphylaxis and blunt therapeutic response to adrenaline; however, β -blockers should never be abruptly discontinued, nor left out in patients with cardiovascular conditions for which taking β -blockers is critical. Some data suggests that angiotensin-converting enzyme (ACE) inhibitors may interfere with compensatory physiologic responses to anaphylaxis, and may augment bradykinin-induced vascular changes, therefore perioperative discontinuation of ACE inhibitors must be weighed against potential benefits per each case as well. Hypovolemia should be avoided (Ledford 2017, Bevanda et al. 2017).

Drugs that stimulate mast cells and basophil histamine release (e.g. morphine, vancomycin, NMBAs) should be given as slowly as possible, never simultaneously with other drugs, and, if available and/or applicable, drugs that do not possess such characteristics should be given instead. Intraoperative antibiotics should be given in the same manner, with loading doses preferably being administered prior to anaesthesia, and not concomitantly with anaesthetics (Ledford 2017).

Ideally, baseline total serum tryptase levels verification prior to anaesthesia/surgery/other medical procedure may help identify patients with clonal mast cell disorders (>11 ng/mL) or mastocytosis (>20 ng/mL), who then require additional precautions (Schwartz 2006).

Finally, other modalities of anaesthesia may be considered in contrast to general anaesthesia, thus avoiding the use of NMBAs and hypnotics – additionally, patients may be awake and communicate symptoms (e.g. pruritus, dyspnoea). However, many types of surgery still require general anaesthesia, in which case volatile anaesthetics should be used if possible, as allergy to these has never been described (Mertes et al. 2009). Local anaesthesia, including peripheral nerve blocks may be adequate in some settings. Patients can be tested prior to being administered local anaesthetic to ensure there is no evidence of IgE-mediated allergy (Levy & Ledford 2017).

Spinal or epidural anaesthesia can be used for procedures below the diaphragm, however this produces sympathectomy below the level of induction of anaesthesia, thus reducing the baseline blood pressure and responsiveness to catecholamines, should the anaphylaxis occur (Mills et al. 2014).

Preinduction management and precautions

An operating theatre should be adequately equipped (and staffed) for management of predictable anaphylaxis. Supplemental oxygen, a cart with airway management equipment, resuscitation drugs and defibrillator should be readily available. Whenever possible, natural rubber equipment/materials should be replaced with polyvinylchloride made equivalents. Also, in ideal circumstances, equipment for taking blood samples should

be available, so that if patient management situation would allow, blood samples could be sent to laboratory to determine tryptase levels for future reference.

At least two large-bored intravenous lines should be inserted and intravenous fluids for volume compensation should be available. Transoesophageal ultrasound might be useful for volume assessment. It is also wise to place an intraarterial cannula for invasive blood pressure monitoring, which could then facilitate immediate intervention in case of blood pressure decrease. Adrenalin, noradrenalin or vasopressin should be prepared if necessary and glucagon can be thought of as well. Concomitantly, anti-H1, anti-H2, glucocorticoids and bronchodilators might be considered in the preoperative planning.

Conclusion

In conclusion, preoperative anaesthesiologic evaluation is of utmost importance for the patient with known previous allergic reactions. A detailed anamnesis is required, with a focus on hypersensitivity reactions, risk factors for anaphylaxis development during the anaesthesia and detection of potential allergic cross-reactivity reactions.

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References

1. Bevanda DG, Cacic M, Mihaljevic S, Bevanda M, Bogut A, Karin M: *Allergic reactions and anesthesia. Psychiatr Danub* 2017; 29:778-786
2. Blumenthal KG & Solensky R: *Choice of antibiotics in penicillin-allergic hospitalized patients. www.uptodate.com*, 2017
3. Butterworth JF, Mackey DC & Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology, 5.ed:McGraw-Hill Education*, 2013
4. Cochico SG: *Propofol allergy: assessing for patient risks. AORN J* 2012; 96:398-408
5. Davenport MS, Asch D, Cavallo J, Cohan R, Dillman JR, Ellis JH et al.: *Manual on Contrast Media – version 10.3. ACR Committee on Drugs and Contrast Media, American College of Radiology* 2017. www.acr.org

6. De Hert S, Imberger G, Carlisle J, Diemunsch P, Fritsch G, Moppett I et al.: Preoperative evaluation of the adult patient undergoing non-cardiac surgery: guidelines from the European Society of Anaesthesiology. *Eur J of Anaesthesiol* 2011; 28:684–722
7. Dewachter P, Mouton-Faivre C, Castells MC & Hepner DL: Anesthesia in the patient with multiple drug allergies: are all allergies the same? *Curr Opin Anesthesiol* 2011; 24:320–325
8. Fisher MM: The preoperative detection of risk of anaphylaxis during anaesthesia. *Anaesth Intensive Care* 2007; 35:899-902
9. Florvaag E, Johansson SGO, Öman H, Venemalm L, Degerbeck F, Dybendalet T et al.: Prevalence of IgE antibodies to morphine. Relation to the high and low incidences of NMBA anaphylaxis in Norway and Sweden, respectively. *Acta Anaesthesiol Scand* 2005; 49:437-444
10. Garvey LH: Allergy and anaesthesia. www.esahq.org, 2011
11. Gonzalez-Uribe V, Navarrete-Rodriguez EM, Sienna-Monge JJ, Del Rio-Navarro BE, Uribe VG, Rodriguez EMN, Sienna-Monge JJ, Rio-Navarro BE: Allergic Reactions in the Perioperative Period in Children. *J Allergy Ther* 2016; 7:238-248
12. Harboe T, Johansson SG, Florvaag E & Oman H: Pholcodine exposure raises serum IgE in patients with previous anaphylaxis to neuromuscular blocking agents. *Allergy* 2007; 62:1445-50
13. Harper NJN, Dixon T, Dugué P, Edgar DM, Fay A, Gooi HC et al.: Suspected anaphylactic reactions associated with anaesthesia. *Anaesthesia* 2009; 64:199-211
14. Harper NJN: Propofol and food allergy. *Br J Anaesth* 2016; 116:11-13
15. Hepner DL & Castells MC: Anaphylaxis During the Perioperative Period. *Anesth Analg* 2003; 97:1381–95
16. Hirayama F: Current understanding of allergic transfusion reactions: incidence, pathogenesis, laboratory tests, prevention and treatment. *Br J Haematol* 2013; 160:434-44
17. Krøigaard M, Garvey LH, Menne T & Husum B: Allergic reactions in anaesthesia: are suspected causes confirmed on subsequent testing? *Br J Anaesth* 2005; 95:468–71
18. Kroigaard M, Garvey LH, Gillberg L, Johansson SGO, Mosbech H, Florvaag E et al.: Scandinavian Clinical Practice Guidelines on the diagnosis, management and follow-up of anaphylaxis during anaesthesia. *Acta Anaesthesiol Scand* 2007; 51:655–670
19. Lasser EC, Berry CC, Mishkin MM, Williamson B, Zheutlin N, Silverman JM: Pretreatment with corticosteroids to prevent adverse reactions to nonionic contrast media. *AJR Am J Roentgenol* 1994; 162:523-6
20. Ledford DK: Perioperative anaphylaxis: Evaluation and prevention of recurrent reactions. www.uptodate, 2017
21. Levy JH & Adkinson NF: Anaphylaxis During Cardiac Surgery: Implications for Clinicians. *Anesth Analg* 2008; 106:392–403
22. Levy JH & Ledford DK: Perioperative anaphylaxis: Evaluation and prevention of recurrent reactions. www.uptodate, 2017
23. Liccardi G, Lobefalo G, Di Florio E, Di Iorio C, Occhiochiuso L, Romano L et al.: Strategies for the prevention of asthmatic, anaphylactic and anaphylactoid reactions during the administration of anesthetics and/or contrast media. *J Investig Allergol Clin Immunol* 2008; 18:1-11
24. Mali S: Anaphylaxis during the perioperative period. *Anesth Essays Res* 2012; 6:124
25. Malsy M, Leberle R, Ehehalt K, Sinner B & Hobbhahn J: Anaphylactic reaction 5 minutes after the start of surgery: a case report. *BMC Res Notes* 2015, 8:117
26. Manfredi G, Pezzuto F, Balestrini A, Lo Schiavo M, Montera MC, Pio A et al.: Perioperative Anaphylactic Risk Score for Risk-Oriented Premedication. *Translational Medicine* 2013; 7:12-17
27. Mertes PM, Laxenaire MC & Alla F: Anaphylactic and anaphylactoid reactions occurring during anesthesia in France in 1999-2000. *Anesthesiology* 2003; 99:536-45
28. Mertes MP, Lambert M, Gueant-Rodriguez RM, Aimone-Gastin I, Mouton-Faivre C, Moneret-Vautrin DA et al.: Perioperative anaphylaxis. *Immunol Allergy Clin N Am* 2009; 29:429–451
29. Michalska-Krzyszowska G: Anaphylactic reactions during anaesthesia and the perioperative period. *Anaesthesiol Intensive Ther* 2012; 44:104–111
30. Mills ATD, Sice PJA, Ford SM: Anaesthesia-related anaphylaxis: investigation and follow-up. *Anaesth Crit Care Pain J* 2014; 14:57-62
31. Pichler WJ: An approach to the patient with drug allergy. 2015. www.uptodate.com
32. Schwartz LB: Diagnostic value of tryptase in anaphylaxis and mastocytosis. *Immunol Allergy Clin North Am* 2006; 26:451
33. Scolaro R, Crilly H, Maycock B, McAleer P, Nicholls K, Rose M et al.: Australian and New Zealand Anaesthetic Allergy Group (ANZAAG) Perioperative Anaphylaxis Investigation Guidelines 2017. www.anzaag.com
34. Varrier M & Ostermann M: Fluid composition and clinical effects. *Crit Care Clin* 2015; 31:823-37
35. Woods BD & Sladen RN: Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth* 2009; 103:57–65

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