

Perioperative anaphylaxis: very serious, not so rare, but still neglected and poorly understood

Anafilaxia perioperatória: muito grave, não tão rara, mas ainda negligenciada e pouco conhecida

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Perioperative anaphylaxis is a serious immediate hypersensitivity reaction, with a mortality rate approaching 5% of cases.¹ This figure exceeds the estimates of mortality from other causes of anaphylaxis, which are less than 1%.² Conversely, immediate perioperative reactions are uncommon events, with an incidence ranging from 1:500 to 1:18,600 procedures.¹ The largest case series in the world were generated in the United Kingdom and France, where the incidence was about 1:10,000 procedures.^{3,4} There is only one (single-center, prospective) study conducted in Brazil, which has demonstrated a higher incidence in our setting. The study found 27.9 immediate grade 1 reactions (exclusively cutaneous) per 10,000 procedures and 7 anaphylactic reactions per 10,000 procedures, i.e., 7 times higher than the incidence rate from Western Europe.⁵ This suggests that, despite being an uncommon event, intraoperative anaphylaxis should not be considered a rare event. Nevertheless, anesthesiologists, the physicians who should recognize these reactions and promptly act to prevent fatal outcomes, are not well-informed on the subject.

Moura et al.,⁶ in a study published in this issue of the *Arquivos de Asma, Alergia e Imunologia*, demonstrated serious gaps in anesthesiologists' knowledge, which may compromise care for patients who develop an immediate reaction during the

procedure. Although they obtained a response rate of just over 10% to the online questionnaire sent to anesthesiologists in the state of Sergipe, the authors demonstrated that more than 10% of these specialists did not mention neuromuscular blockers as a possible cause of the reactions. It is important to note that this class of drugs is the most common cause of reactions in many of the published case series.⁷ Furthermore, regarding the management of anaphylaxis, 10.3% of respondents reported using crystalloid resuscitation as the first therapeutic measure in intraoperative anaphylaxis.

Apparently, anesthesiologists have insufficient knowledge not only of intraoperative reactions but also of drug hypersensitivity reactions. In another Brazilian study, published in the proceedings of a local event and presented at the Drug Hypersensitivity Meeting of the European Academy of Allergy and Clinical Immunology (DHM-EAACI 2022),⁸ 104 anesthesiologists completed an online questionnaire. There was clear evidence that current well-established concepts about hypersensitivity to beta-lactam antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs) are unknown to those colleagues. The survey results showed that 40% believed in a high likelihood of cross-reactivity between penicillin and cefazolin, although it is currently known that this

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likelihood is less than 2%. Furthermore, more than 90% of anesthesiologists denied the existence of potential cross-intolerance between dipyrone and other NSAIDs,⁸ with the so-called “non-selective reactors” to NSAIDs clearly being the majority of these patients.

It can be postulated that the limited knowledge of anesthesiologists regarding drug allergy may be, at least in part, attributed to the minimal involvement of faculty members specialized in Allergy and Immunology in undergraduate medical education in Brazil. Most Brazilian medical schools do not have Allergy and Immunology as a course in their curriculum. Allergic and immunological diseases are often taught by other specialties with practical experience in these diseases, such as pediatrics, dermatology, pulmonology, otolaryngology, infectious diseases, and rheumatology, among others. However, some topics such as “Drug Hypersensitivity,” “Food Allergy,” “Anaphylaxis,” and “Inborn Errors of Immunity” encompass more than one organ or system, clearly showing that the participation of Allergy and Immunology specialists in the training of physicians would be of great value.

This deficient knowledge is clearly not limited to specialists in Anesthesiology but rather extends to most physicians who are not specialists in Allergy and Immunology. Two Brazilian studies, conducted in the states of Rio de Janeiro and Alagoas, showed that emergency physicians, although most of them had already treated cases of anaphylaxis during their shifts, were poorly trained and not up-to-date on the management of this life-threatening syndrome.^{9,10}

Regarding intraoperative anaphylaxis, it is important to highlight that, even after completing medical school, the physicians who specialize in anesthesiology (and who will deal with these complications) seem to continue to have little interaction with our specialty. Two medical societies, the Brazilian Association of Allergy and Immunology (ASBAI) and the Brazilian Society of Anesthesiology (SBA), have put a great deal of effort into improving the continuing medical education of their specialists. These societies have been collaborating, interacting during their annual congresses, and generating joint scientific production on the topic of perioperative hypersensitivity.^{11,12} However, these efforts still prove insufficient. We need to do more to reach colleagues who work face-to-

face with the patients who experience these severe reactions during surgery. This will lead to a reduction in morbidity and mortality from these events and to the correct referral of these cases to allergists and immunologists for investigation.

References

1. Volcheck GW, Melchior BB, Farooque S, Gonzalez-Estrada A, Mertes PM, Savic L, et al. Perioperative Hypersensitivity Evaluation and Management: A Practical Approach. *J Allergy Clin Immunol Pract.* 2023 Feb;11(2):382-392. doi: 10.1016/j.jaip.2022.11.012.
2. Pouessel G, Dribin TE, Tacquard C, Tanno LK, Cardona V, Worm M, et al. Management of Refractory Anaphylaxis: An Overview of Current Guidelines. *Clin Exp Allergy.* 2024 Jul;54(7):470-88. doi: 10.1111/cea.14514.
3. Harper NJN, Cook TM, Garcez T, Farmer L, Floss K, Marinho S, et al. Anaesthesia, surgery, and life-threatening allergic reactions: epidemiology and clinical features of perioperative anaphylaxis in the 6th National Audit Project (NAP6). *Br J Anaesth.* 2018;121:159-71.
4. Mertes PM, Alla F, Tréchet P, Auroy Y, Jouglu E. Anaphylaxis during anesthesia in France: an 8-year national survey. *J Allergy Clin Immunol.* 2011;128:366-73.
5. Garro LS, Aun MV, Soares ISC, Ribeiro MR, Motta AA, Kalil J, et al. Specific questionnaire detects a high incidence of intra-operative hypersensitivity reactions. *Clinics (Sao Paulo).* 2018 May 17;73:e287. doi: 10.6061/clinics/2018/e287.
6. Moura IVS, Cunha-de-Castro MEP, Macedo ACL, Falheiros BBO. Manejo da anafilaxia perioperatória sob a visão dos anestesiolistas. *Arq Asma Alerg Imunol.* 2024;8(3):213-24.
7. Garvey LH, Ebo DG, Mertes PM, Dewachter P, Garcez T, Kopac P, et al. An EAACI position paper on the investigation of perioperative immediate hypersensitivity reactions. *Allergy.* 2019 Oct;74(10):1872-84. doi: 10.1111/all.13820.
8. Torquato MC, Takaoka F, Rizzo LV, Vieira JE, Aun MV. Practical management of anesthesiologists regarding hypersensitivity reactions to drugs in the perioperative period. *Einstein (São Paulo).* 2021;19(Suppl 1):S50.
9. Fonseca CSBM, Moraes IC, Contin IN, Maeda LH, Uehara MK, Almeida MEC, et al. Anafilaxia: conhecimento médico sobre o manejo em anafilaxia. Estudo em urgentistas na cidade de Petrópolis - RJ. *Rev Bras Alerg Imunopatol.* 2009;32(1):9-12.
10. Santos TP, Almeida GRF, Lins LC, Moreira IFM. Atendimento a pacientes com anafilaxia: conhecendo as principais condutas médicas nos setores de urgência e emergência dos hospitais da cidade de Maceió, Alagoas. *Braz J Allergy Immunol.* 2014;2:231-4.
11. Spindola MAC, Solé D, Aun MV, Azi LMTA, Bernd LAG, Garcia DB, et al. Update on perioperative hypersensitivity reactions: joint document of the Brazilian Society of Anesthesiology (SBA) and Brazilian Association of Allergy and Immunology (ASBAI) - Part I: post-crisis guidelines and treatment. *Braz J Anesthesiol.* 2020 Sep-Oct;70(5):534-548. doi: 10.1016/j.bjan.2020.06.004.
12. Solé D, Spindola MAC, Aun MV, Araújo Azi LMT, Bernd LAG, Garcia DB, et al. Update on perioperative hypersensitivity reactions: joint document from the Brazilian Society of Anesthesiology (SBA) and Brazilian Association of Allergy and Immunology (ASBAI) - Part II: etiology and diagnosis. *Braz J Anesthesiol.* 2020 Nov-Dec;70(6):642-61. doi: 10.1016/j.bjan.2020.08.008.