

Management of perioperative anaphylaxis from the anesthesiologist perspective

Manejo da anafilaxia perioperatória sob a visão dos anestesiológicos

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ABSTRACT

Perioperative anaphylaxis is a severe systemic reaction that can occur at any point during the surgical procedure, typically minutes after induction of anesthesia, and can also be caused by agents administered via other routes (such as chlorhexidine, latex, and methylene blue). Global epidemiology suggests an increase in the incidence of drug-induced anaphylaxis, highlighting the need for improved diagnosis and management of this condition. This study aims to describe anesthesiologists' knowledge of perioperative anaphylaxis management. This is a descriptive, exploratory, quantitative study conducted from May to October 2023. Data were collected through an online questionnaire aimed at assessing anesthesiologists' knowledge of triggering agents, risk factors, clinical manifestations, diagnosis, treatment, and prevention of perioperative anaphylaxis. The questionnaire was developed based on a review of the literature on the topic. The study included 29 anesthesiologists. Although anesthesiologists were aware of certain etiologic agents involved in anaphylaxis, 10.3% of them did not mention neuromuscular blockers, and only 48.3% considered chlorhexidine an option. Only 27.6% and 6.9% identified female sex and beta-blocker use as significant risk factors. Hypotension was reported as the main clinical manifestation by 93.7% of participants. The use of epinephrine for treatment was reported by 89.7%, and despite the lack of convincing evidence, 48.3% of anesthesiologists recommended the use of corticosteroids. No significant difference in scores was found between those who graduated in anesthesiology more than 5 years ago and those who graduated less than 5 years ago, nor in relation to age, first contact with the topic, or years of experience as a specialist. No significant differences were found in scores related to the variables of interest. Many participants had deficient knowledge of perioperative anaphylaxis, posing a potential risk to patients.

Keywords: Anaphylaxis, hypersensitivity, anesthesia, intraoperative complications, perioperative period.

RESUMO

A anafilaxia perioperatória é uma reação sistêmica grave que pode ocorrer em qualquer período durante as etapas cirúrgicas, geralmente minutos após a indução anestésica, podendo ocorrer também com agentes administrados por outras vias (como clorexidina, látex e azul de metileno). A epidemiologia global sugere um aumento na incidência da anafilaxia induzida por drogas, destacando a necessidade de melhoria no diagnóstico e manejo de tal condição. O objetivo deste artigo é descrever o conhecimento sobre o manejo da anafilaxia perioperatória pelos anestesiológicos. Trata-se de um estudo descritivo, exploratório, quantitativo, realizado de maio a outubro de 2023. Os dados foram coletados via questionário online e visou avaliar o conhecimento dos anestesiológicos sobre agentes desencadeantes, fatores de risco, manifestações clínicas, diagnóstico, tratamento e prevenção da anafilaxia perioperatória. O questionário foi construído após revisão da literatura sobre as principais informações acerca do tema. Participaram da pesquisa 29 anestesiológicos. Apesar de haver conhecimento acerca de determinados agentes etiológicos envolvidos na anafilaxia, 10,3% dos anestesiológicos não assinalou os bloqueadores neuromusculares e apenas 48,3% considerou a clorexidina como opção. Apenas 27,6% e 6,9% indicou o sexo feminino e o uso de medicamentos betabloqueadores como fatores de risco relevantes. A hipotensão foi descrita como principal manifestação clínica por 93,7% dos participantes. O uso de adrenalina no tratamento foi afirmado por 89,7% e, apesar de não haver evidências convincentes, 48,3% dos médicos indicou o uso de corticoide. Não houve diferença significativa de pontuação entre formados em anesthesiologia há mais de 5 anos e formados há menos de 5 anos, nem em relação à idade, primeiro contato com o tema ou tempo de atuação como especialista. Não foram encontradas diferenças significativas nas pontuações relativas às variáveis avaliadas. Muitos participantes apresentaram déficits no conhecimento sobre anafilaxia perioperatória, representando um risco potencial para os pacientes.

Descritores: Anafilaxia, hipersensibilidade, anestesia, complicações intraoperatórias, período perioperatório.

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Introduction

The safety of anesthetic procedures has increased significantly in recent decades, but they are still considered high-risk. This is due to the fact that several medications are administered simultaneously or near-simultaneously over a short period of time. Among potential anesthesia-related complications, immediate hypersensitivity reactions to drugs—which may or may not be allergic in nature—stand out. When such reactions are severe and occur during the perioperative period, they are known as intraoperative or perioperative anaphylaxis.¹

Perioperative anaphylaxis is a rare hypersensitivity reaction that may occur at any time during the patient's surgical experience, most commonly within minutes of intravenous administration of an anesthetic agent, but also to agents administered by other routes (such as chlorhexidine, latex, and methylene blue) due to absorption through the skin, mucosa, or tourniquet removal.²⁻⁴

These reactions pose a diagnostic and clinical challenge, due to their wide range of clinical manifestations and the multiple underlying mechanisms involved. This is compounded by the technical limitations of the perioperative environment, which amplify the complexity of diagnosis. The capacity for objective assessment to identify hypersensitivity reactions is also greatly restricted in the anesthetized patient.^{5,6}

Epidemiological data suggest an increase in the global incidence of drug-induced anaphylaxis, which highlights the urgency of improving allergy reporting systems. The incidence of anaphylaxis is estimated to range from 1 in 386 to 1 in 13,000 anesthetic procedures³, which translates into 1 case for every 7 years of professional activity over an anesthesiologist's career; mortality rates vary between approximately 3% and 10%. This wide variation in incidence rates is mainly attributable to a lack of uniform clinical and diagnostic criteria, as well as to the diversity of studied populations.^{3,6-8}

Due to the low incidence of perioperative anaphylaxis, this serious condition is often unexpected by anesthesiologists and is sometimes neglected by those who fail to identify it and to provide immediate, appropriate treatment—which explains its high mortality rate. In addition to the difficulty in recognizing this condition, a lack of hospital protocols to guide the approach to perioperative anaphylaxis makes the extremely complex management of this disorder even more challenging.⁹

Analysis of anesthesiologists' knowledge about perioperative anaphylaxis can provide important inputs to inform the scientific community regarding how this condition is diagnosed and managed in practice. Furthermore, it encourages an early approach to anaphylaxis.

Given the complexity of clinical diagnosis of perioperative anaphylaxis, compounded by the absence of protocols to assist anesthesiologists in managing this complication, the objective of this study is to describe the knowledge of anesthesiologists working in private and public settings regarding the diagnosis and management of patients with perioperative anaphylaxis.

Methods

This is a descriptive, exploratory, quantitative study, carried out entirely in a virtual environment, from May through October 2023. Data were collected with a questionnaire (Appendix 1) posted on the Google Forms platform and designed to assess anesthesiologists' knowledge about perioperative anaphylaxis. The questionnaire was constructed after a literature review of core information on the topic.

The sample of interest consisted of anesthesiologists working in the state of Sergipe, Brazil. Contact with prospective participants was established through the Sergipe Anesthesiologists Cooperative (Coopanest-SE), which maintains a registry of and information on all anesthesiologists practicing in the state. Participants showed interest in taking part in the study by signing an Informed Consent Form (ICF).

Approval was obtained from the Universidade Federal de Sergipe Research Ethics Committee (Certificate of Submission for Ethical Appraisal: 66854822.2.0000.0217) before any study procedures were performed. The study was conducted in accordance with the guidelines of Brazilian National Health Council Resolution No. 466/12. Only those prospective participants who had signed an ICF were allowed to take part. To ensure anonymity, neither the form nor the database contained any nominally identifying information. Strict confidentiality was also preserved regarding the information acquired, and respondents were free to choose to refuse to participate in the study if they felt uncomfortable in any way.

The Google Forms survey link was divided into sections. The first section consisted of the ICF, presented with the options “I agree” (which allowed respondents to proceed to the survey) and “I do not agree” (which terminated their participation). The subsequent sections presented the questionnaire itself (Appendix 1), with the second section consisting of seven questions to characterize the sample while the third and fourth sections addressed the pathophysiology, clinical presentation, and management of perioperative anaphylaxis.

The third section consisted of three questions. Question 1 listed 10 agents potentially related to perioperative anaphylaxis. Question 2 listed 15 risk factors potentially related to this condition. Question 3 listed 15 potential clinical manifestations of perioperative anaphylaxis. In this third section, participants were asked to select the items that they believed to be associated with perioperative anaphylaxis; they were required to select at least 1 item in each question. The fourth section of the questionnaire presented 8 multiple-choice questions about the diagnosis, treatment, and prevention of perioperative anaphylaxis.

The level of knowledge of the respondents was calculated based on their scores for the last two sections. The third section score ranged from 3 to 40 points, while the fourth section score ranged from 0 to 80 points. Final assessment of the level of knowledge was based on the sum score for sections three and four, with a minimum of 3 points and a maximum of 120 points.

Collected data were tabulated in Microsoft Excel (version 16.3) and analyzed in Jamovi (version 2.3). Absolute (n) and relative (%) frequency measures were generated and the Shapiro-Wilk test was used to verify the normality of distribution of the variables of interest. Spearman's correlation test was used for quantitative variables with a non-normal distribution.

Comparison of knowledge scores in relation to seniority (time since completion of training) was performed using the Mann-Whitney test after dividing the sample into two groups (> 5 years or < 5 years since graduation). The Kruskal–Wallis test was used to analyze the timing of first contact with the topic of perioperative anaphylaxis.

Results

Invitations were sent to the 261 anesthesiologists who met the criteria for inclusion. Of these, only 29

(11%) agreed to take part in the study, of whom 20 (69%) were under age 40 and had < 10 years of experience. The sample profile is described in Table 1.

Table 1

Sample profile of anesthesiologists in the state of Sergipe, Brazil

Characteristics of the sample		
Age range	N	%
31-40	20	69.0
41-50	6	20.6
> 50	3	10.3
Year of completion of anesthesiology training	N	%
1990-2000	3	10.3
2001-2010	4	13.8
2011-2020	18	62.0
> 2020	4	13.8
Years in practice	Public health care facilities	Private facilities
< 5 years	9	9
5-10 years	11	11
11-15 years	3	2
> 15 years	6	7

* The maximum variation in years worked in public vs. private facilities for the same respondent was 3 years.

Most participants had been practicing as anesthesiologists for at least 5 years (96.6%) and had diagnosed at least one case of perioperative anaphylaxis (65.5%). Medical residency was the first point of contact with the topic of perioperative anaphylaxis for 21 (72.4%) participants.

Regarding specific knowledge about perioperative anaphylaxis, no participants achieved the maximum score of 120 points; scores ranged from 64 to 114 points among the respondents, with an average score of 85.9.

The results were distributed into percentiles, with the 25th percentile (p25) delimited by a score of 76, the 50th percentile (p50) by a score of 88, and the 75th percentile (p75) by a score of 92. Table 2 shows the distribution of scores across the percentiles described above.

Table 2

Perioperative anaphylaxis knowledge score achieved by anesthesiologists in the state of Sergipe, Brazil

Score achieved	Percentile	N	%
< 76	< 25	7	24.1
76-87	25-50	7	24.1
88-92	50-75	5	17.2
> 92	> 75	10	34.4

The sample was divided into anesthesiologists with more than 5 years of experience and those with less than 5 years of experience (time since completion of anesthesiology training), with the intention of assessing whether this parameter would interfere with the scores achieved. Anesthesiologists with more than 5 years of experience had an average score of 84, while those with less than 5 years of experience had an average score of 90; the difference was not statistically significant ($p = 0.21$). This analysis was hampered by the small number of respondents with < 5 years of training. The average score among anesthesiologists who encountered perioperative anaphylaxis for the first time during medical residency was 86.28, while the group who first came into contact with the topic during medical school had an average score of 86.57 ($p = 0.5$). The number of years of practice as an anesthesiologist in public and/or private hospitals, year of completion of anesthesiology training, and age had no influence on scores.

Regarding agents possibly implicated in perioperative anaphylaxis, all respondents identified antibiotics and latex-derived products as such, while 28 (96.6%) selected non-steroidal anti-inflammatory drugs, 26 (89.7%) selected neuromuscular blocking agents, and 17 (58.6%) selected opioids. The most well-known risk factors were frequency of exposure,

selected by 28 respondents (96.6%); asthma, selected by 27 respondents (93.1%); and food allergy, chosen by 26 respondents (89.7%). The frequency of selection of other agents and risk factors is shown in Tables 3, 4, and 5.

Regarding the diagnosis of anaphylaxis, all participants reported being aware that the surgical environment can make the manifestations of perioperative anaphylaxis less readily apparent, and the vast majority (96.6%) stated that the diagnosis of perioperative anaphylaxis is a clinical one. Regarding laboratory tests, 16 (55.1%) of respondents reported not knowing whether an increase in tryptase could occur in anaphylaxis or not being familiar with this test at all.

When asked about the treatment of anaphylaxis, 26 (89.7%) responded that epinephrine should be the first medication to be administered, while 3 (10.3%) answered that crystalloids should be administered first. According to 23 (79.3%) of the participants, the dose of epinephrine should be chosen according to the severity of the patient's clinical condition, and 14 (48.3%) believed that early administration of steroids and antihistamines could improve clinical outcomes.

Regarding preventive management in patients who had recent episodes of perioperative anaphylaxis, 27 (93.1%) of respondents stated that proper management would be to refer the patient to an immunologist for a skin test; only 2 (6.9%) would perform a skin test immediately after the patient's recovery. As for management after diagnosis and reversal of the initial episode of perioperative anaphylaxis, 22 (75.9%) would opt for admission to an intensive care unit and observation for 24 hours, while 7 (24.1%) would keep the patient under observation for 6 hours on a regular ward.

Discussion

This is the first study to assess and describe the knowledge of anesthesiologists regarding diagnosis and management of perioperative anaphylaxis in Brazil, a topic that is often neglected and insufficiently discussed, including by academic institutions and specialists. Similar studies have been carried out in Petrópolis (state of Rio de Janeiro)¹⁰ and Maceió (state of Alagoas)¹¹; these, however, investigated physicians' knowledge about the management of anaphylaxis overall (not limited to perioperative anaphylaxis) in the urgent care/emergency department setting.

Table 3

Agents that anesthesiologists believed to be associated with perioperative anaphylaxis

Agent	N	%
Latex-derived products (e.g., sterile gloves and urinary catheters)	29	100
Antibiotics (e.g., cephalosporins and penicillins)	29	100
Non-steroidal anti-inflammatory drugs (NSAIDs)	28	96.6
Neuromuscular blocking agents (e.g., rocuronium and vecuronium)	26	89.7
Local anesthetics	18	62.1
Dyes (e.g., methylene blue)	18	62.1
Opioids (e.g., morphine and pethidine)	17	58.6
Chlorhexidine	14	48.3
Hypnotics (e.g., propofol)	14	48.3
Heparin	11	37.9

Table 4

Risk factors that anesthesiologists believed to be associated with perioperative anaphylaxis

Risk factors	N	%
Frequency of exposure to antigen	28	96.6
Asthma or history of asthma	27	93.1
Food allergies	26	89.7
Multiple surgical procedures	25	86.2
Family history of atopy	24	82.8
Parenteral administration of antigen	20	69.0
Systemic mastocytosis	19	65.5
Time of exposure to antigen	18	62.1
Female sex	8	27.6
Chronic lung disease (e.g., COPD)	6	20.7
Recent intracranial surgery and hyperthyroidism	5	17.2
On angiotensin-converting enzyme inhibitors (ACEi)	4	13.8
Cardiovascular disease	3	10.3
On beta blockers	2	6.9

COPD = Chronic obstructive pulmonary disease.

Table 5
Clinical manifestations that anesthesiologists believed to be associated with perioperative anaphylaxis

Clinical manifestation	N	Percentage (%)
Angioedema	27	93.1
Hypotension	27	93.1
Cutaneous manifestations	27	93.1
Hypoxemia (desaturation)	23	79.3
Urticaria	22	75.9
Cardiac arrest (pulseless)	21	72.4
Dyspnea	24	82.8
Tachycardia	20	69.0
Bradycardia	14	48.3
Decreased EtCO ₂	13	44.8
Cyanosis	13	44.8
Nausea	11	37.9
Vomiting	11	37.9
Rhinorrhea	10	34.5
Abdominal pain	7	24.1

EtCO₂ = end-tidal carbon dioxide.

IgE-mediated anaphylactic reactions can be triggered by various agents. Neuromuscular blockers are the most frequently reported in most studies, followed by latex and antibiotics.^{2,12} Although most respondents reported that neuromuscular blockers are a cause of anaphylaxis, 10.3% did not select this option, thus failing to recognize one of the main factors involved in immune-mediated reactions in the perioperative period.¹³ No data were found from other studies to compare whether anesthesiologists from other regions share this perception.

NSAIDs are a recognized cause of drug-induced anaphylaxis, although rarely in the perioperative setting.¹⁴ The *6th National Audit Project* (NAP 6), the largest study of anaesthesia- and surgery-related anaphylaxis, found only one case of ibuprofen-induced anaphylaxis in 356 European hospitals.¹⁴ However, despite being an uncommon cause of perioperative anaphylaxis, NSAIDs do play a major role in anaphylaxis overall. In the Latin American literature, they are often cited as the main cause of non-allergic anaphylactic reactions. In a study by the Latin

American Society of Allergy, Asthma and Immunology (SLAAI) with 634 participants from 15 Latin American countries, 31.2% of systemic anaphylactic reactions were drug-induced, with 22.7% of these cases being attributed to NSAIDs.¹⁵ In a large Brazilian study, aspirin, metamizole, and diclofenac were the drugs most commonly implicated in non-allergic anaphylactic reactions.¹⁶ Given this epidemiology, it is justified that 28 (96.6%) of our respondents considered NSAIDs as possible causes of perioperative anaphylaxis.¹⁶

Regarding chlorhexidine, NAP 6 reported an increase in the role of this substance and of contrast agents in perioperative anaphylaxis. In the United Kingdom, chlorhexidine was identified as the third most common cause of perioperative anaphylaxis. In Asia and Belgium, it was the fourth leading cause.¹⁷ Despite the substantial number of reactions associated with this compound, only 14 (48.3%) respondents in our sample believe that chlorhexidine can be implicated in immediate hypersensitivity reactions in the perioperative period.

Due to the large number of possible agents, the causal factor is never identified in approximately half of all cases, which has implications for the subsequent prevention of these reactions.³ In addition, there are exceedingly rare triggers of anaphylactic reaction, such as heparin^{2,13,18}, which despite being implicated in few cases, was named as a possible trigger by 11 (37.9%) respondents.

Female sex is one of the leading risk factors, with a threefold higher incidence of perioperative anaphylaxis in this group compared to male patients. This difference only occurs during childbearing age, which suggests a relationship with sex hormones.¹⁹⁻²¹ Despite its importance, this factor was recognized by only 8 (27.6%) respondents.

A history of asthma, food allergies, multiple surgical procedures, family history of atopy, and frequency of antigen exposure were recognized as potential risk factors by more than 80% of anesthesiologists in the survey. These are also important factors, but are more relevant in the pediatric population.^{14,19-21} Systemic mastocytosis, time of exposure to antigen, and parenteral administration of the antigen are known to be associated with an increased risk of perioperative anaphylaxis^{14,21}; however, less than 70% of respondents recognized them as such.

Comorbidities that may contribute to greater severity of anaphylaxis include cardiovascular diseases, chronic lung diseases, hyperthyroidism, and recent intracranial surgery.² The latter, despite being cited in several articles, lacks robust evidence proving its relationship with a worse prognosis. The mechanism is unclear, but it has been suggested that such surgeries may disrupt the integrity of the blood-brain barrier, potentially increasing permeability to various substances²² and thus predisposing to an exacerbated inflammatory response and a greater risk of cerebral edema. Furthermore, the release of inflammatory mediators such as bradykinin, histamine, and substance P can compromise blood–brain barrier junctions, facilitating the passage of potentially harmful agents.^{23,24}

In addition to comorbidities, some medications such as ACE inhibitors and beta blockers are also considered to increase the severity of symptoms and reduce the response to treatment.^{19-21,25} Furthermore, studies have shown that the odds ratio for developing anaphylaxis is 6.8 when on beta blockers and 13 when on ACE inhibitors. However, other studies have indicated that they are significant risk factors only when used simultaneously; further research is needed

to analyze the impact of these medications as risk factors.^{21,26,27}

Although many reports in the literature mention the aforementioned factors as being associated with the severity of perioperative anaphylaxis, comorbidities were reported by less than 25% of our participants, and use of medications by less than 15%, with the use of beta blockers being recognized as a risk factor by only 2 (6.9%) respondents. It is possible that part of the sample failed to select these options because there is still ongoing debate about the actual impact of these drugs.

The main signs and symptoms of anaphylaxis and the objective diagnostic criteria for its diagnosis are highly varied, with a wide range of possible presentations; the major manifestations are cardiovascular, respiratory, and cutaneous. Hypotension is found in most, if not all, patients with perioperative anaphylaxis.²⁵ This sign was recognized by 93.7% of respondents, as were cutaneous manifestations and angioedema. The latter, despite being absent in some cases or even going unnoticed when the patient is covered by surgical drapes, were present in 70% of IgE-mediated reactions and in 95% of non-IgE reactions in a 2011 French study.^{13,28} Cutaneous manifestations were considered to be among the most common by 27 of the 29 respondents.

A study published in 2015 reported that cardiac arrest is the only sign of anaphylactic reaction in 51.7% of cases², although this has not been replicated in other research; 72.4% of our respondents were aware that this is a possible presentation of perioperative anaphylaxis. Bronchospasm is another common sign, present in 49% of cases in the United Kingdom and 43% in the USA, potentially manifesting as cyanosis, dyspnea, hypoxemia, and reduced end-tidal carbon dioxide (EtCO₂).^{2,25,29} Among our respondents, 79.3% selected hypoxemia with desaturation, 69% selected dyspnea, and only 44.8% considered cyanosis and reduced EtCO₂ as possible signs of perioperative anaphylaxis.

Hypotension, tachycardia, and bradycardia may be merely side effects of anesthetic agents rather than manifestations of anaphylaxis, and, although common, tachycardia may not occur in anaphylactic reactions in patients who are on beta blockers. Furthermore, patients with severe hypovolemia may not present with tachycardia with hypotension but rather with bradycardia, due to the Bezold–Jarisch reflex.^{19,30} Intuitively, tachycardia, being a more common manifestation of anaphylaxis, was reported by 69%

of participants; conversely, less than half (48.3%) believe that bradycardia is among the most common symptoms of this reaction.

Stated by several authors and very well consolidated in the literature, masking of the clinical manifestations of perioperative anaphylaxis by the surgical environment^{18,25} was recognized by 100% of participants in this survey. The concept that diagnosis of this condition is clinical¹⁸ was also recognized by the majority of the sample (96.6%).

Although the diagnosis is indeed based on the signs and symptoms exhibited by the patient, there are laboratory tests that can assist in the workup of a suspected reaction, such as tryptase—one of the mediators released by the mechanisms of drug-induced anaphylaxis, whether IgE-mediated or otherwise, due to degranulation of mast cells and basophils.²⁵ However, tryptase levels may increase under other conditions and, therefore, false-positive results are possible.²

When assessing knowledge about this alternative method of diagnosis, we found that 37.9% of respondents were not even aware of this test, and only 37.9% gave a response consistent with the literature. The low level of knowledge of this option among anesthesiologists is justified, as all guidelines agree that laboratory tests are not useful for the diagnosis of anaphylaxis, due to the delay in measuring mediators such as total serum tryptase. Furthermore, this test is largely unavailable in clinical practice in both the public and private sectors, given that there is no provision for its coverage by insurance companies in Brazil.³¹

Regarding management of anaphylaxis, 89.7% of respondents selected epinephrine as the first-line drug of choice medication, while 10.3% stated that intravenous crystalloids should take precedence. In the Petrópolis study, 63.4% of anesthesiologists cited epinephrine as their first-line drug of choice¹⁰, versus 78.9% of those in the Maceió study¹¹, corroborating our findings. According to the literature, epinephrine should always be the first drug administered in cases of anaphylaxis, since its alpha- and beta-adrenergic effects have a broad effect on the pathophysiological mechanisms of anaphylaxis—reducing edema, urticaria, and upper airway obstruction; promoting bronchodilation; and suppressing mediators generated by the degradation of mast cells and basophils.³²

Despite its narrow therapeutic window, failure to use epinephrine appropriately outweighs any of its adverse effects, even in patients with heart disease;

the heart is a target organ for anaphylaxis – the released mediators can cause myocardial infarction and/or arrhythmias – even without administration of epinephrine, so there is no contraindication to its use.³¹

Other measures do include resuscitation with intravenous fluids, although this should not be the first action taken.^{18,25}

The most recent studies on the management of anaphylaxis provide no evidence that corticosteroids and antihistamines improve clinical outcomes; therefore, these drugs should not be a priority.³² Antihistamines can reduce itching and edema, but despite causing smooth muscle relaxation, they are unable to relieve bronchospasm. Corticosteroids have an anti-inflammatory effect with onset of action between 4-6 hours, and are thus not effective in an anaphylactic emergency.³³ Furthermore, a systematic review of 31 studies suggests that use of corticosteroids for the prevention of biphasic reactions is not recommended, as there is no convincing evidence and well-known adverse effects.³²

Nevertheless, 48.3% of our respondents stated that steroids improve clinical outcomes, which is inconsistent with the published evidence. These drugs can be used to reduce symptoms once the patient is stable, although it should be noted that there are no studies demonstrating their benefits and that adverse effects such as worsening hypotension have been reported.

Regarding management after stabilization of the patient, 22 (75.9%) respondents would opt for admission to an intensive care unit and observation for 24 hours, while 7 (24.1%) would keep the patient under observation for 6 hours on a regular ward. According to the literature, patients must remain under observation in an intensive care unit (ICU) setting for at least 6-8 hours if the anaphylactic reaction involved respiratory symptoms alone and for 12-24 hours if there were cardiovascular manifestations. After all, biphasic reactions—a recrudescence of symptoms without further exposure to the precipitating trigger—occur in up to 20% of cases, are unpredictable, and can last up to 36 hours.¹⁸

Based on the data collected herein, most participants scored high on the perioperative anaphylaxis knowledge questionnaire. Nevertheless, a substantial portion of the sample demonstrated outdated knowledge on this topic, failing to recognize the agents most commonly responsible for anaphylactic

reactions and advocating for the use of corticosteroids and antihistamines, which is still controversial. Furthermore, the failure to identify known risk factors and the failure to use epinephrine as the first-line drug of choice may jeopardize patient management and prognosis.

One limitation of this study was the low questionnaire response rate, which means our sample may not accurately reflect the knowledge of anesthesiologists on this topic. Despite the small sample and use of a questionnaire that has yet to be validated, our findings highlight an urgent need for greater attention to perioperative anaphylaxis. It is imperative that new studies be conducted and continuously updated strategies be developed to mitigate the risks associated with this condition in the surgical setting. Finally, promoting a more effective collaboration between medical specialties is crucial for advancing and enhancing knowledge on this topic.

References

- Aun MV, Garro LS, Ribeiro MR, Motta AA, J Kalil, Giavina-Bianchi P. Anafilaxia perioperatória: A experiência brasileira. *Rev Port Imunoalergol*. 2016 Jun;24(2):99-106.
- Valencia MIB. Anafilaxia perioperatoria. *Rev Bras Anestesiol*. 2015;65(4):292-7. doi: <https://doi.org/10.1016/j.bjan.2014.09.002>.
- Kosciuczuk U, Knapp P. What do we know about perioperative hypersensitivity reactions and what can we do to improve perioperative safety? *Ann Med*. 2021 Jan;53(1):1772-8.
- 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: <https://doi.org/10.1111/all.13820>.
- Ebo DG, Mertes PM, Garvey LH, Dewachter P, Scherer K, Luyckx J, et al. Molecular mechanisms and pathophysiology of perioperative hypersensitivity and anaphylaxis: a narrative review. *Br J Anaesth*. 2019 Jul;123(1):49.
- Di Leo E, De Gregorio C, Cavaliere G, De Re V. Focus on the agents most frequently responsible for perioperative anaphylaxis. *Clin Mol Allergy*. 2018;16(1):19.
- Vorobeichik L, Weber EA, Tarshis J. Misconceptions Surrounding Penicillin Allergy. *Anesth Analg*. 2018 Sep;127(3):642-9.
- Villén FE, Navas SS. Anafilaxia en anestesia. *Rev Esp Anestesiol Reanim*. 2013;60:55-64.
- Laguna J, Archilla J, Doña I, Corominas M, Gastaminza G, Mayorga C, et al. Practical guidelines for perioperative hypersensitivity reactions. *J Investig Allergol Clin Immunol*. 2018 Aug;28(4):216-32.
- 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.
- 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.
- Silva WA, Macêdo Pinheiro A. Reações anafiláticas em anestesia. *J Surg Clin Res*. 2020 May 22;11(1):66-72.
- Tacquard C, Iba T, Levy JH. Perioperative anaphylaxis: reply. *Anesthesiology*. 2023 May 29;139(3):362-4.
- Filho AAMT, Castro MEPC de. Perfil epidemiológico das principais drogas e substâncias relacionadas à etiologia da anafilaxia perioperatória no Brasil e no mundo: uma revisão literária. *Braz J Health Rev*. 2021 May 17;4(3):10695-716.
- Solé D, Ivancevich JC, Borges MS, Coelho MA, Rosário NA, Arduso LRF, et al. Anaphylaxis in Latin America: a report of the online Latin American survey on anaphylaxis (OLASA). *Clinics*. 2011 Jun;66(6):943-7.
- Aun MV, Blanca M, Garro LS, Ribeiro MR, Kalil J, Motta AA, et al. Nonsteroidal anti-inflammatory drugs are major causes of drug-induced anaphylaxis. *J Allergy Clin Immunol Pract*. 2014 Jul-Aug;2(4):414-20. doi: [10.1016/j.jaip.2014.03.014](https://doi.org/10.1016/j.jaip.2014.03.014).
- Cook TM, Harper NJN, Farmer L, Garcez T, Floss K, Marinho S, et al. Anaesthesia, surgery, and life-threatening allergic reactions: protocol and methods of the 6th National Audit Project (NAP6) of the Royal College of Anaesthetists. *Br J Anaesth*. 2018 Jul;121(1):124-33.
- Yim R. World Federations Societier of Anesthesiologists. ATOTW tutorial. 2016;324:1-6.
- Caffarelli C, Stringari G, Pajno GB, Peroni DG, Franceschini F, Iacono ID, et al. Perioperative allergy: risk factors. *Int J Immunopathol Pharmacol*. 2011 Jul;24(3 Suppl):27-34.
- Mirone C, Preziosi D, Mascheri A, Micarelli GL, Farioli L, Balossi LG, et al. Identification of risk factors of severe hypersensitivity reactions in general anaesthesia. *Clin Mol Allergy*. 2015 Jun 22;13(1):16.
- Solé D, Spindola MAC, Aun MV, Azi LA, Bernd LAG, Bianchi D, et al. Abordagem das reações de hipersensibilidade perioperatória: orientações da Sociedade Brasileira de Anestesiologia e da Associação Brasileira de Alergia e Imunologia - Parte II: etiologia e diagnóstico. *Arq Asma Alerg Imunol*. 2020;4(3):112-29.
- Oldfield EH, Merrill MJ. Blood-brain barrier disruption in the treatment of brain tumors: clinical implications. *J Neurosurg*. 1996 Dec;85(6):1056-64. doi: [10.3171/jns.1996.85.6.1056](https://doi.org/10.3171/jns.1996.85.6.1056).
- Kadry H, Noorani B, Cucullo L. A blood-brain barrier overview on structure, function, impairment, and biomarkers of integrity. *Fluids Barriers CNS*. 2019 Dec 18;16(1):6. DOI: <https://doi.org/10.1186/s12987-019-0134-6>.
- Lee J, Rabai F. Blood-Brain Barrier. *OpenAnesthesia* [Internet]. 2023 Mar 4. Available from: <https://www.openanesthesia.org/keywords/blood-brain-barrier/>. Acessado em: 09/09/2024.
- Long E, Kaufman D, Clark P, McLeod M. Recognition, treatment, and prevention of perioperative anaphylaxis: a narrative review. *AIMS Med Sci*. 2022;9(1):32-50.
- Smith MA, Newton LP, Blanch MAB, Cuervo-Pardo L, Cho L, Newton D, et al. Risk for anaphylactic reaction from cardiac catheterization in patients receiving beta-adrenergic blockers or angiotensin-converting enzyme-inhibitors. *J Allergy Clin Immunol Pract*. 2020;8(6):1900-5. doi: [10.1016/j.jaip.2019.10.020](https://doi.org/10.1016/j.jaip.2019.10.020).
- Huang W, Li X, Xiang Y, Li J, Zhou X, Zheng X, et al. Risk factors and prevention for perioperative anaphylaxis: a nested case-control study. *Int J Clin Pharm*. 2019 Dec;41(6):1442-50. doi: [10.1007/s11096-019-00902-7](https://doi.org/10.1007/s11096-019-00902-7).
- Mertes PM, Alla F, Tréchet P, Auroy Y, Jouglé E. Anaphylaxis during anesthesia in France: an 8-year national survey. *J Allergy Clin Immunol*. 2011 Aug;128(2):366-73.
- LoVerde D, Iweala OI, Eginli A, Krishnaswamy G. Anaphylaxis. *Chest*. 2018 Feb;153(2):528-43.
- Kalangara J, Vanijcharoenkarn K, Lynde GC, McIntosh N, Kuruvilla M. Approach to perioperative anaphylaxis in 2020: updates in diagnosis and management. *Curr Allergy Asthma Rep*. 2021 Jan;21(1):4.

31. Simons FER, Arduzzo LRF, Bilo MB, Cardona V, Ebisawa M, El-Gamal YM. International consensus on anaphylaxis. *World Allergy Organ J.* 2014;7:9.
32. Sociedade Brasileira de Pediatria, Departamento Científico de Alergia. Guia Prático de Atualização - Anafilaxia: atualização 2021 [Internet]. 2021. Available from: https://www.sbp.com.br/fileadmin/user_upload/22970c-GPA-Anafilaxia_-_Atualizacao_2021.pdf
33. Figueira MCBS, Sarinho ESC. Uso de corticoides e anti-histamínicos na prevenção da anafilaxia: uma revisão bibliométrica. *Arq Asma Alerg Imunol.* 2017;1(4):335-41.

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Appendix 1

Questionnaire to assess anesthesiologists' knowledge of perioperative anaphylaxis

**Management of perioperative anaphylaxis from the perspective of anesthesiologists
in the state of Sergipe, Brazil**

SAMPLE PROFILE

Age: _____ Year of completion of Anesthesiology training: _____

1 - Of your time practicing as an anesthesiologist, how long has been spent in public and private practice? Fill in below as follows:

Public _____ years Private _____ years

Note: if you spent less than 1 year in either, enter "0" (zero)

2 - Have you practiced as an Anesthesiologist in the last 5 years?

☐ Yes ☐ No

3 - Have you ever diagnosed a case of perioperative anaphylaxis?

☐ Yes ☐ No

4 - Do you feel confident in diagnosing a case of perioperative anaphylaxis?

☐ Yes ☐ No

5 - When did you first become aware of the topic of perioperative anaphylaxis? _____

☐ Medical school ☐ Residency ☐ Congress/Course/Conference ☐ Other: _____**QUESTIONNAIRE**

Description: The European Academy of Allergy and Clinical Immunology defines anaphylaxis as a severe, life-threatening, generalized or systemic hypersensitivity reaction. Perioperative anaphylaxis is a systemic reaction that occurs during induction of anesthesia, within minutes of intravenous (IV) administration of induction agents. However, certain agents administered by other routes may also cause such a reaction, during maintenance of anesthesia (approximately 15 minutes after induction) or during recovery (due to absorption through the skin or mucosa or removal of tourniquets).

1 - Based on your knowledge as an anesthesiologist, select the option(s) that describe agents you believe to be associated with Perioperative Anaphylaxis:

- ☐ Neuromuscular blocking agents (e.g., rocuronium and vecuronium)
- ☐ Latex-derived products (e.g., sterile gloves and urinary catheters)
- ☐ Antibiotics (e.g., cephalosporins and penicillins)
- ☐ Chlorhexidine
- ☐ Hypnotics (e.g., propofol)
- ☐ Opioids (e.g., morphine and pethidine)
- ☐ Non-steroidal anti-inflammatory drugs (NSAIDs)
- ☐ Heparin
- ☐ Local anesthetics
- ☐ Dyes (e.g., methylene blue)

2 - Based on your knowledge as an anesthesiologist, select the option(s) that describe risk factors you believe to be associated with Perioperative Anaphylaxis:

- ☐ Cardiovascular disease
- ☐ Chronic lung disease (e.g., COPD)
- ☐ Recent intracranial surgery
- ☐ Hyperthyroidism
- ☐ Multiple surgical procedures
- ☐ Female sex
- ☐ Asthma or history of asthma
- ☐ Food allergies
- ☐ Family history of atopy
- ☐ Systemic mastocytosis
- ☐ On angiotensin-converting enzyme inhibitors (ACEi)
- ☐ On beta blockers
- ☐ Time of exposure to antigen
- ☐ Frequency of exposure to antigen
- ☐ Parenteral administration of antigen

Appendix 1 (continuation)

Questionnaire to assess anesthesiologists' knowledge of perioperative anaphylaxis

3 - Among the potential manifestations of anaphylaxis, which are most common in cases of perioperative anaphylaxis?

(You may select more than one choice)

- ☐ Urticaria
- ☐ Angioedema
- ☐ Hypotension
- ☐ Cardiac arrest (pulseless)
- ☐ Dyspnea
- ☐ Hypoxemia (desaturation)
- ☐ Decreased EtCO₂
- ☐ Cyanosis
- ☐ Abdominal pain
- ☐ Nausea
- ☐ Vomiting
- ☐ Rhinorrhea
- ☐ Tachycardia
- ☐ Bradycardia
- ☐ Cutaneous manifestations

4 - Can general anesthesia, as well as the surgical environment, make the manifestations of perioperative anaphylaxis less apparent?

- ☐ Yes
- ☐ No
- ☐ I don't know

5 - Based on your opinion as an anesthesiologist, is perioperative anaphylaxis a clinical diagnosis?

- ☐ Yes
- ☐ No
- ☐ I don't know

6 - In your opinion, can perioperative anaphylaxis be diagnosed from an elevated total plasma tryptase measurement in a single (spot) specimen?

- ☐ Yes
- ☐ No
- ☐ I don't know
- ☐ I am unfamiliar with this test

7 - In your opinion, among the medications listed below, which should be the first-line drug of choice for management of perioperative anaphylaxis?

- ☐ Epinephrine
- ☐ Intravenous crystalloids
- ☐ Norepinephrine
- ☐ Glucagon
- ☐ Vasopressin
- ☐ Glucocorticoids
- ☐ Antihistamines
- ☐ Other

8 - When administering epinephrine for treatment of perioperative anaphylaxis, does the dose depend on the severity of anaphylaxis and should it be titrated to clinical response?

- ☐ Yes
- ☐ No
- ☐ I don't know

9 - Does early administration of steroids (e.g., dexamethasone, hydrocortisone) and antihistamines in the treatment of perioperative anaphylaxis improve clinical outcomes?

- ☐ Yes
- ☐ No
- ☐ I don't know

10-Regarding preventive management of patients who have had a recent episode of perioperative anaphylaxis, which of the following is recommended?

- ☐ Refer to an immunologist for skin testing
- ☐ Perform a skin test immediately after the patient recovers
- ☐ Neither skin tests nor any preventive measures are necessary

11-After diagnosis and reversal of a first episode of perioperative anaphylaxis, what would be your subsequent management?

- ☐ Immediate discharge with referral to an allergist
- ☐ Observation for 6 hours on a regular ward
- ☐ Observation for 24 hours in the intensive care unit