

PERIOPERATIVE ANAPHYLAXIS: A SYSTEMATIC REVIEW

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Abstract

Background: Perioperative anaphylaxis can be associated with antibiotics, neuromuscular blocking agents, dyes, latex, and disinfectants. This article evaluates the condition's epidemiology, pathophysiology, and treatment, including an allergy assessment.

Aim: This investigation aims to investigate the possibility that perioperative anaphylaxis develops.

Methods: The study met the PRISMA 2020 guidelines through self-evaluation. The investigators ensured the study's current became feasible. Publications from 2015 to 2023 were searched using various online reference databases, including Pubmed and SagePub. Excluded were review papers, pre-existing publications, and incomplete articles.

Result: The search generated 552 and 321 articles in the PubMed and SagePub databases, respectively. 54 articles were found for PubMed and 21 for SagePub in the investigation conducted for the last year of 2015. A total of 18 papers were collected, with 12 generated from PubMed and 6 from SagePub. We included five studies that met the criteria.

Conclusion: The presence of anesthetics, surgical settings, and various medications and substances may complicate the process of accurate diagnosis. A systematic approach was used to identify the reaction, perpetrator, and future management. Effective management of perioperative anaphylaxis requires close coordination among anesthesiology, surgery, and allergy specialists.

Keyword: Allergy; Anaphylaxis; Hypersensitivity; Perioperative

INTRODUCTION

"Allergic reaction" refers specifically to a response mediated by IgE antibodies. IgE attaches to basophils and mast cells, prompting the release of chemical mediators that can harm nearby tissue upon exposure to antigens.¹ Type I hypersensitivity, also known as allergy, is an immunological condition characterized by a heightened sensitivity of the body to generally immunogenic or atopic substances. Non-atopic individuals do not experience the same sensitivity to foreign substances or environmental factors as those with atopic conditions.²⁻⁴

Anaphylaxis is a potentially fatal reaction that can occur suddenly and has a mortality rate of 3-9%. Its incidence during anesthesia is estimated to be 1 in 1,250-20,000 cases worldwide.⁵ Anesthesia-related allergic responses commonly manifest as hypotension during induction, tachycardia following intubation, and bronchospasm caused by physical activation of the airways.⁶

Allergic reactions may manifest shortly after allergen exposure as well as commonly after the administration of certain medications. This leads to cardiac arrhythmias, collapse, and hypotension. In their study of 732 hospital mortality, Ebbsen et al. determined that 18.2% were associated with adverse drug reactions.⁷ Perioperative anaphylaxis is a life-threatening condition stimulated by antibiotics, neuromuscular blocking agents, coloring substances, latex, and chemical disinfectants. The article provides updated information on epidemiological studies, disease progression, cause-and-effect agents, and management principles, including a comprehensive allergy analysis.⁸⁻¹¹

This study aims to investigate anaphylaxis incidences in surgical procedures.

METHODS

The study followed the PRISMA 2020 guidelines to ensure its validity and dependability. The study found perioperative anaphylaxis, emphasizing the importance of timely ability through prior research evaluation. The article highlights the significance of resolving the raised concerns to accomplish the study's objective.

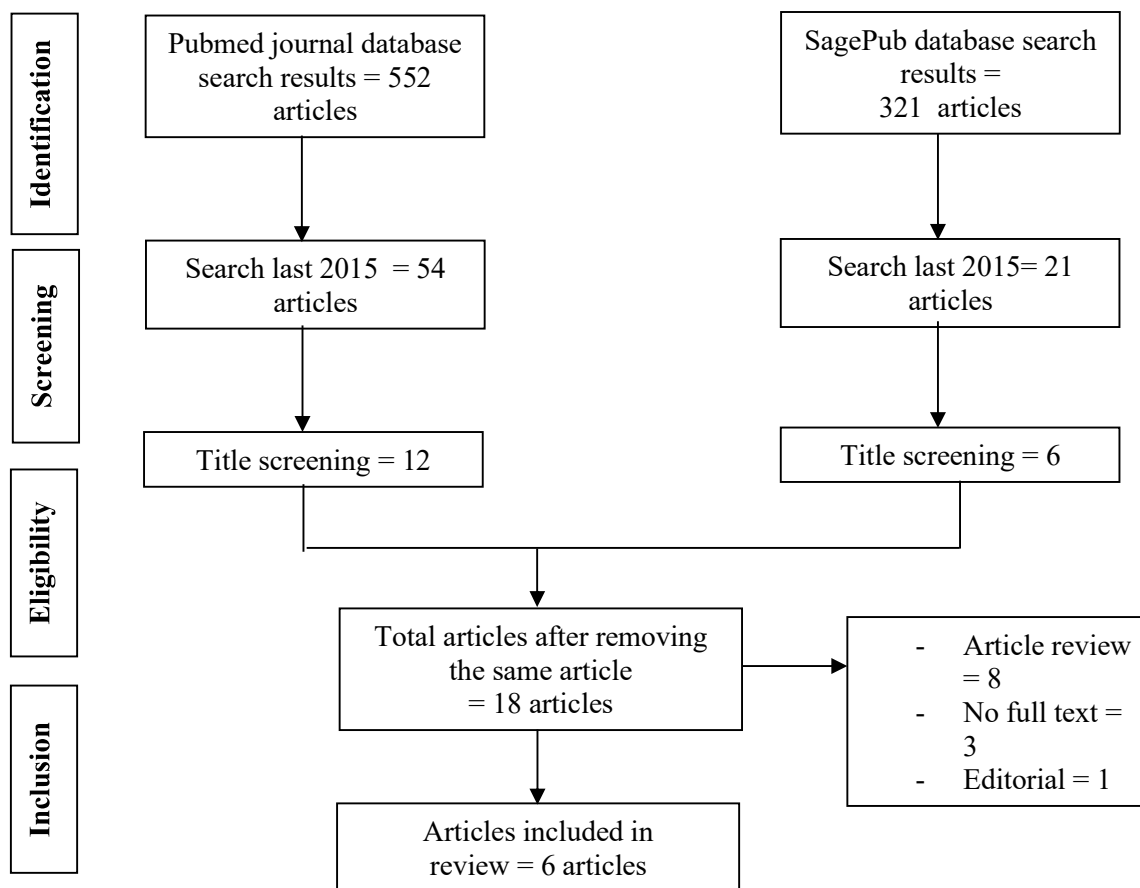


Figure 1. Article search flowchart

To be included in the study, researchers must meet specific requirements, including writing the paper in English and focusing primarily on perioperative anaphylaxis. Publications between 2015 and the evaluation period will be included in the assessment. Editorials, applications without a DOI, already published review articles, and submissions that are essentially exact copies of previously published journal articles are a few examples of research that cannot be published. We used between “perioperative” and “anaphylaxis” as keywords. The search for studies to be included in the systematic review was carried out from June, 9th 2023 using the PubMed and SagePub databases by inputting the words: (“perioperative”[All Fields] OR “perioperatively”[All Fields]) AND (“anaphylaxis”[MeSH Terms] OR “anaphylaxis”[All Fields]) used in searching the literature.

We assessed the validity of each study by examining its abstract and title. They investigated other historical documents. This conclusion is based on a meta-analysis of studies that utilized identical methods. Submissions must be written in unpublished English. The systematic review only included works that met specific predetermined criteria. Thus, the search results are limited. The analysis of the research findings needs to be revised. Here is the breakdown. The paper provides information on the authors, publication date, study location, subject characteristics, research topic, and study parameters. The report includes author and publication date details. Endnote eliminated duplicate results from the list. Two evaluators analyzed the article titles and abstracts. The research examined comprehensive literature to ascertain qualifications and provide information on GWG and additional health issues. The justices decided through deliberation. Authors screen papers by reviewing their abstracts and titles before conducting a thorough analysis. The subsequent stage involves screening documents that satisfy the inclusion criteria and identifying review topics based on subject expertise. This approach applies to both research and review articles.

RESULT

The PubMed database generated 552 articles, while SagePub generated 321 articles in response to our search. 54 articles were found on PubMed and 21 on SagePub for 2015. A total of 18 papers were collected, with 12 sourced from PubMed and 6 from SagePub. We included five research studies that met the criteria.

Harper, et al (2018)¹⁰ reported an estimated incidence of 1 in 10,000 for anesthesia-related events. Excluding cases caused by indicating postpones or insufficient evidence may result in a 70% increase in incidence. Among the 199 offenders were chlorhexidine (18), patent blue coloring (9), neuromuscular blocking medication (65), antibiotics (94), and chlorhexidine (18). Teicoplanin contributed to 38% of cases of anaphylaxis induced by antibiotics, despite only being responsible for 12% of antibiotic exposures. The antibiotic test doses had an impact on 18 individuals. Succinylcholine-induced anaphylaxis, primarily characterized by bronchospasm, exhibited a higher incidence rate than other neuromuscular blocking agents, with a twofold increase. Atracurium-induced anaphylaxis is characterized by hypotension. Non-depolarizing neuromuscular blocking agents demonstrated similar incidents. No reports of local anesthesia or latex-induced allergy were found.¹²

The most common symptoms noticed were hypotension (46%), bronchospasm (18%), tachycardia (9.8%), oxygen desaturation (4.7%), bradycardia (3%), and reduced/absent capnography trace (2.3%). All patients indicated hypotension. Rapid neuromuscular blocking agents, antibiotics, and chlorhexidine administration were observed, while Patent Blue dye was comparatively delayed. There were 40 instances of cardiac arrest resulting in 10 fatal accidents. Cardiac arrest typically manifests as pulseless electrical activity accompanied by bradycardia. Worse outcomes were associated with ASA, obesity, beta-blockers, and ACE inhibitors. The hospital incident reporting system received 70% of cases, while the Yellow Card Scheme of the Medicines and Healthcare Products Regulatory Agency received 24%.¹⁰

Liu, et al (2022)¹² study revealed that perioperative anaphylaxis occurred in 109 out of 145 patients, with cardiovascular symptoms being the primary clinical feature. Neuromuscular blocking agents accounted for the majority of cases (32.1%). Following the diagnostic workup, 52 patients underwent a repeat procedure without experiencing anaphylaxis recurrence.

Table 1. The literature include in this study

Author	Origin	Method	Sample	Result
Harper, 2018 ¹⁰	United Kingdom (UK)	Retrospective study	266 reports	It was estimated that there was one case of perioperative anaphylaxis for every 10,000 times that anesthesia was administered.
Liu, 2022 ¹²	China	Retrospective study	145 patients	According to the study, neuromuscular blocking agents are the primary cause of anaphylaxis during the perioperative period. Allergy diagnostic tests are essential for patients to identify the allergen responsible for their reaction and seek alternative anesthetics in the future.
Zuo, 2020 ¹³	China	Retrospective study	109 patients	Although the risk of allergic reactions to laxatives is low, patients with a history of drug hypersensitivity reactions (DHR) should undergo allergy testing. Skin testing and basophil activation tests aid in the clinical diagnosis of authentic laxative allergies.
Au, 2020 ¹⁴	Hong Kong	Retrospective study	60 patients	Performing a thorough investigation following an intraoperative anaphylactic event has a reasonable likelihood of identifying the causative allergen. These findings have implications for patient management and the planning of subsequent anesthetic procedures.
Zhang, 2021 ¹⁵	China, Japan, United State of America (USA)	Retrospective study	5,078,118 surgical procedures	According to the results of this nationwide survey, the incidence of perioperative anaphylaxis was one in 11,360, however the results differed greatly from area to region. The fundamental cause of this pattern is still a mystery; nevertheless, it may be attributed to the influences of either the environment or genetics; therefore, additional research is required.
Suigiya, 2023 ¹⁶	Japan	Prospective study of perioperative anaphylaxis	43 patients	The clinical signs and therapies of perioperative anaphylaxis might vary, and the decision on the administration of epinephrine is determined by the severity of the patient's symptoms.

Zuo, et al (2020)¹³ study was conducted with a sample size of 109 patients. The primary cause for referral was suspected drug hypersensitivity reactions (DHR) following procedures involving local anesthetics (n=68, 62%). A history of DHR followed this to other drugs and the requirement for local anesthetics in upcoming procedures (n=41, 38%). Out of the 68 patients suspected of having a DHR to LAs, only six were confirmed to have a genuine allergy based on positive skin tests and BAT. Furthermore, all 41 patients who had previously experienced drug hypersensitivity reactions to other medications tested negative.

Au, et al (2020)¹⁴ study was conducted with a sample size of 60 patients. Tryptase was evaluated in 81.7% (49/60) of subjects, with the majority (71.4%, 35/49) demonstrating elevated levels. The study found that 79.7% of the participants had positive results, with the tryptase-positive category having the highest yield at 88.6%. The skin test, the most sensitive test, revealed a positive impact in 79.6% of individuals. Neuromuscular blockers and antibiotics accounted for the highest percentages of intraoperative anaphylaxis, at 25.0% and 23.3%, respectively. Allergies were detected based on reaction time. Most neuromuscular blocker reactions happened during induction, whereas all gelofusine allergies occurred during the maintenance of anesthesia. 21.7% of the participants underwent general anesthesia after their initial exposure without exhibiting any allergic reactions.

Zhang, et al (2021)¹⁵ The study included 447 cases out of 5,078,118 surgical procedures. The incidence of perioperative anaphylaxis in China was estimated to be 1 case per 11,360 anesthetics, with a 95% confidence interval ranging from 1 case per 12,521 to 1 case per 10,397 anesthetics. The incidence of the studied phenomenon was higher in South China (1 in 6050; 95% CI, 1:8013 to 1:4859) compared to Northeast China (P<0.01). Hypotension (91.1%) and tachycardia (65.3%) were the most common symptoms observed. 83.4% of the subjects were administered epinephrine. CPR was required by 6.0% (n=27) of the patients. The mortality rate was 2.0%, with 9 cases. The study revealed a global incidence of perioperative anaphylaxis at a rate of 1 in 11,360 cases, with significant regional variability. The etiology of this trend warrants further investigation to determine whether genetic or environmental factors influence it.

Cardiovascular indications were the most prevalent among the 43 patients examined in this study, as reported by another study. The median duration between symptom onset and anaphylaxis diagnosis was 10 minutes, ranging from 5.0 to 17.8 minutes. The utilization rates of epinephrine were 30.2% for unused, 48.8% for intravenous, and 20.9% for intramuscular administration. The median duration between diagnosis of anaphylaxis and administration of epinephrine was 7 minutes, with an interquartile range of 1.5 to 8.0 minutes. Antihistamines and corticosteroids were used in 69.8% of patients who received i.v. Epinephrine had a higher worst shock index (2.77 [0.90] / mean [standard deviation]) compared to those who did not receive epinephrine (1.35 [0.41]) or those who received i.m. epinephrine (1.89 [0.77] (P <0.001)).¹⁶

DISCUSSION

Perioperative anaphylaxis (PA) is an uncommon yet potentially fatal condition that can occur during surgical procedures. Perioperative responses of a severe nature can occur at a frequency ranging from 1 in 7000 to 10,000. Treatment implies patient stabilization and identification of the causative agent. Proper identification is essential for avoiding future complications and preventing unnecessary medication allergy identification.^{8,17}

Perioperative hypersensitivity responses (POH) pose clinical and diagnostic challenges due to their diverse clinical manifestations and multiple pathomechanisms. POH may not elicit an allergen-specific immune response through cross-linking mast cell and basophil sIgE antibodies.⁴ POH is a condition that affects multiple bodily systems, including circulatory, respiratory, and integumentary. Complement-derived anaphylatoxins and off-target mast cell, basophil, or surface receptor occupancy cause it. This pertains to surgical or procedural pathology and impacts pre-existing physiological capacity. The cardiovascular system can compensate for intraoperative anaphylaxis, but severe allergies can lead to circulatory failure due to maldistribution and hypovolemia, which limit venous return: epinephrine and i.v. Fluids are necessary for resuscitation, but excessive administration without volume expansion can be detrimental. The pathophysiology of bronchospasm involves neural airway control, and premedication with anticholinergics is advantageous. Pulmonary edema can be caused by pulmonary capillary hypertension, alveolocapillary membrane incompetence, or a combination of both. Angioedema can be either histaminergic or non-histaminergic, with the latter being bradykinin-mediated. Managing and investigating POH cases necessitates comprehending their molecular etiology and pathophysiology.¹⁸

To perform a precise assessment, identify possible exposures such as pharmaceuticals, sanitizers, latex, and colorants and opt for practical examinations. Standard testing methods involve measuring tryptase levels and conducting skin tests using non-irritating doses of drugs and substances administered during therapy. These tests ascertain the causative agent of the adverse reaction.^{11,19} Perioperative anaphylaxis, mediated by IgE, is mainly attributed to intravenous medications, particularly neuromuscular blocking agents (NMBAs) and antibiotics. NAP6 research showed that antibiotics were implicated in 48% of cases studied, while NMBAs were involved in 25%. Co-amoxiclav and teicoplanin represent 90% of the discovered antibiotics. Teicoplanin was frequently administered in more than 50% of cases, as patients self-reported penicillin allergies, although the integrity of those reports was hardly confirmed.¹⁰

Perioperative anaphylaxis, mediated by IgE, can be caused by drugs such as iodinated contrast agents, sugammadex, iodinated dyes, antiseptics, colloids, and dyes. Chlorhexidine-induced anaphylaxis has become more prevalent in

Denmark, the UK, and Belgium while remaining infrequent in France. Latex allergy was not reported during the NAP6 survey due to its infrequency.^{10,12}

CONCLUSION

The presence of anesthetics, surgical conditions, and various pharmacological agents can complicate the diagnosis process. A systematic approach is utilized to identify the reaction, perpetrator, and future management. Effective management of perioperative anaphylaxis requires close coordination among anesthesiology, surgery, and allergy specialists.

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