



PATIENTS WITH ALLERGIES – PREOPERATIVE PREPARATION AND PREMEDICATION

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ABSTRACT:

Purpose: The study investigates the need and effectiveness of preoperative prick test corticosteroids as antiallergic premedication for patients with a history of allergic reactions undergoing surgery under general anesthesia, focusing on hypersensitivity reactions (HSRs).

Material and Methods: A prospective clinical-epidemiological study was conducted with 60 patients, divided into groups receiving corticosteroid premedication (30 patients) and no premedication (30 patients). Patients had histories of allergies, and hypersensitivity was monitored intraoperatively and postoperatively. Data were analyzed using various statistical methods to assess the impact of corticosteroid use and prick tests.

Results: The study revealed no significant reduction in the incidence of mild or moderate-to-severe HSRs with corticosteroid premedication. Allergic reactions, including rash and bronchospasm, were observed in three patients despite receiving corticosteroids. Additionally, the absence of corticosteroid or H1/H2 blocker premedication did not increase the incidence of HSRs in other patients. Statistical analysis demonstrated a lack of correlation between premedication and the prevention of allergic reactions. The study proved that prick tests are not a reliable method to identify possible triggers of HSRs

Conclusion: Corticosteroid premedication does not effectively prevent perioperative HSRs in patients with allergic conditions. The study suggests that routine use of corticosteroids for this purpose should be reconsidered. A detailed allergy history is crucial for identifying at-risk patients, rather than prick tests and national protocols for managing perioperative HSRs reactions should be developed.

Keywords: Hypersensitivity Reactions, Perioperative Care, Anesthesia, Anaphylaxis, Premedication, Allergy,

INTRODUCTION

Hypersensitivity reactions, particularly anaphylaxis, are among the most serious complications encountered during the perioperative period. Although relatively rare, these reactions can be life-threatening, accounting for 5–7% of anesthesia-related deaths globally. Patients undergoing anesthesia are exposed to a variety of drugs and substances, including anesthetics, antibiotics, muscle relaxants, and analgesics, which can trigger allergic or non-allergic HSRs. Diagnosing and managing these reactions is particularly challenging, as anesthetized patients cannot report typical warning symptoms such as dizziness, hoarseness, or difficulty breathing.

One of the most common strategies to prevent HSRs are preoperative prick tests and the administration of corticosteroid premedication. However, there is growing evidence that this approach may not provide the protective effect traditionally attributed to it. While corticosteroids are known for their anti-inflammatory and immunosuppressive properties, their efficacy in preventing perioperative allergic reactions remains questionable. In fact, recent studies suggest that corticosteroid premedication may neither reduce the incidence nor the severity of HSRs.

Aim:

This study aims to evaluate the effectiveness of preoperative prick tests and corticosteroid premedication in preventing perioperative hypersensitivity reactions in patients with a history of allergic conditions.

Tasks:

- To investigate if preoperative prick tests are reliable in predicting triggers for perioperative HSRs
- To investigate the incidence and severity of perioperative HSRs in patients receiving corticosteroid premedication.
- To analyze the relationship between corticosteroid premedication and the occurrence of allergic reactions.
- To assess whether corticosteroid premedication effectively prevents mild to severe HSRs.
- To provide recommendations for the management

of perioperative allergic patients based on clinical evidence and study results.

By addressing these objectives, the study seeks to contribute to the development of safer and more evidence-based protocols for the prevention and management of perioperative hypersensitivity reactions.

Anesthesiologists routinely administer anesthesia across various clinical settings for procedures like surgery, intensive care, and invasive interventions. Anesthesia introduces patients to numerous foreign substances, such as anesthetics, analgesics, antibiotics, antiseptics, and blood products, which can lead to adverse reactions (AR), including HSRs and anaphylaxis. Adverse reactions are classified into type A and type B reactions. Type A reactions are common, predictable, and dose-dependent, while type B reactions (hypersensitivity) are rare, unpredictable, and less dose-dependent. These hypersensitivity reactions can be immediate (within minutes to 6 hours) or delayed (over 6 hours), ranging from mild (urticaria, gastrointestinal symptoms) to severe, life-threatening reactions like anaphylaxis. [1, 2]

Perioperative HSRs vary in severity, classified from grades 1 to 5, with grades 3-5 being life-threatening anaphylaxis. During the perioperative period, the estimated incidence of HSRs is 1 in 10,000 anesthetic procedures. However, prospective studies suggest this is underestimated, citing frequencies of 1:3,180 and 1:1,480. A recent prospective Spanish study found a perioperative reaction incidence of 1:381, with 48% of cases being mild (affecting only the skin) and 52% being anaphylaxis. In most series, allergic reactions account for at least 60% of all perioperative hypersensitivity reactions observed during the perioperative period. Recently, an analysis of three different French databases provided a national estimate of the incidence of immediate IgE-mediated allergic reactions during anesthesia. This report confirms the general opinion that immediate HSRs are largely underreported, with the incidence of allergic reactions estimated at 1,006 per million procedures. Perioperative anaphylaxis's approximate frequency is 1 in 10,000–20,000 anesthetic procedures. In other sources, the incidence of perioperative anaphylaxis is reported to be approximately 1:7,000–10,000, with mortality rates ranging from 1.4% to 4.8%. The incidence is thought to range from 1 in 3,500 to 1 in 20,000 surgeries, with mortality rates between 3% and 9%. It should also be noted that there is a lack of data on the incidence of perioperative HSRs in many countries. Anaphylaxis during surgery accounts for 9–19% of surgical complications globally and 5–7% of anesthesia-related deaths. The two main causes of death from anaphylaxis are laryngeal angioedema and cardiocirculatory collapse. Secondary brain damage resulting from anoxia is the most significant morbidity, occurring in about 2% of patients affected by anaphylaxis. Patients under anesthesia will not exhibit symptoms of severe allergic reactions, such as hoarse voice, dysphagia, dizziness, or blurred vision. Despite their severity, many hospitals lack standardized protocols for managing these

reactions, leading to challenges in diagnosis, treatment, and reporting. [3, 4, 5, 6, 7, 8, 9]

Risk factors for perioperative allergic reactions include drug-related triggers for IgE-mediated allergies and patient-specific factors. A history of previous perioperative HSRs is the strongest predictor, increasing the risk of allergic reactions or anaphylaxis by 5 to 6 times. Patients who have experienced moderate (e.g., urticaria, mild bronchospasm) to severe (e.g., shock, respiratory or cardiac arrest) reactions are particularly at risk. Other factors include advanced age, female gender, race, and type of surgery, with women having a threefold higher likelihood of perioperative reactions than men. Latex hypersensitivity is more common in children, while adult hypersensitivity tends to peak in women around age 40 and men over age 50. Comorbidities such as chronic lung disease, coagulopathy, malignancy, obesity, and coronary artery disease further raise the risk. Special care is needed for patients with conditions like asthma, atopy, mastocytosis, and angioedema. Common triggers of perioperative anaphylaxis include muscle relaxants, beta-lactam antibiotics, latex, chlorhexidine, and certain colloids. Less frequent triggers include NSAIDs, heparin, and oxytocin. Chlorhexidine-containing products should be avoided in allergic individuals, and perioperative stress or infections can also act as cofactors in triggering HSRs. [10, 11, 12, 13, 14, 15]

Perioperative anaphylaxis is challenging to diagnose due to the simultaneous use of multiple drugs, the overlapping effects of various anesthetic agents with hypersensitivity characteristics (e.g., hypotension), and the patient's inability to report symptoms while under anesthesia. Hypersensitivity reactions most frequently occur intraoperatively during the induction and maintenance phases of anesthesia (80%), while they are significantly less common postoperatively (in the post-anesthesia care unit or surgical ward) (20%). The most common reactions occur within the first 5 minutes of induction (86% of cases), while reactions occurring between 5-10 minutes and 10-20 minutes account for only 4% of cases. A study on fatal anaphylaxis reports that the average time to cardiac arrest is 5 minutes after intravenous injection, 15 minutes after subcutaneous injection, and 30 minutes after oral intake. Generally, for the most common triggers (neuromuscular blockers and antibiotics), symptoms appear within the first 30 minutes of anesthesia. When symptoms begin after the 30th minute, the primary cause typically involves chlorhexidine, latex, contrast agents, plasma expanders, blood products, and Sugammadex. [16, 17, 18, 19]

The European Academy of Allergy and Clinical Immunology's Drug Allergy Group has published recommendations for investigating perioperative allergic reactions. However, in most countries, there are no protocols for managing patients with a history of perioperative HSRs, which may increase the potential risk of re-exposure to allergens. The most appropriate approach is to identify these patients during the pre-anesthesia consultation and refer them to an allergist for evaluation. Clini-

cal history is crucial for diagnosing perioperative immediate HSRs, and the Ring and Messmer scale is useful for describing clinical characteristics. All grades (I-IV) on this scale require further investigation. In France and the U.S., combined measurements of acute plasma histamine and tryptase are recommended, while only tryptase measurement is used in Scandinavia, the UK, Australia, New Zealand, and Spain. Skin tests remain the “gold standard” for identifying the triggering agent and determining the underlying pathophysiological (allergic vs. non-allergic) mechanism, forming the basis for recommendations for future anesthesia. Skin tests require experience and time and are best performed in specialized clinics. Since no proven effective preventive therapeutic strategies exist, vigilance on the part of treating physicians for rapid recognition and treatment of these reactions, along with subsequent allergological investigations to identify the cause and prevent recurrences, is crucial. Every patient with a history of previous anaphylaxis or a severe reaction during anesthesia should be referred to an allergologist to identify the trigger. Currently, there is no evidence supporting the predictive value of skin tests for anaphylactic reactions, and systematic screening of the general population is not recommended, except for patients in recognized risk groups. These risk groups are identified as follows: 1) patients who had an unexplained reaction to an unidentified allergen during previous anesthesia, 2) patients, who are known to be allergic to drug classes that will be used during the anesthesia period, and 3) patients at risk of latex allergy. Referral for allergy testing is strongly recommended for patients with a prior episode of perioperative hypersensitivity, as a history of previous hypersensitivity reactions or unexplained perioperative events is the only confirmed risk factor for future episodes. The presence of atopy, food allergies, other drug allergies, previous uneventful anesthesia, or a family history of anesthesia or drug allergies is not considered independent risk factors for perioperative HSRs. [15, 16, 19, 20, 21]

To prevent recurrence of acute allergic-like reactions, premedication has been introduced for individuals requiring repeated administration of triggering medications. A meta-analysis by Hsieh et al. demonstrated that in patients who had previous HSRs, it was significantly less likely for them to develop ones after premedication. Several strategies for premedication to prevent HSRs in high-risk patients have been proposed, primarily involving combinations of corticosteroids and/or antihistamines. The typical recommendations include administering corticosteroids and/or antihistamines according to specific protocols that vary between institutions. Premedication with corticosteroids is widely used in clinical practice to reduce the formation of drug antibodies, and antihistamines are used to prevent or mitigate allergic reactions. However, a meta-analysis of ten studies did not demonstrate any benefit from premedication with corticosteroids or antihistamines alone or in combination in reducing the risk of acute infusion reactions in pa-

tients. Also, few randomized controlled trials exist, and there is no strong evidence that premedication reduces the risk of life-threatening anaphylaxis. There are mixed results regarding the use of antihistamines or corticosteroids as premedication in patients with mastocytosis. Currently, corticosteroids are not recommended as a preventive treatment for AR, partly because of their debated effectiveness and partly due to the fact that corticosteroid premedication can mask or delay the recognition and subsequent treatment of perioperative anaphylaxis.

Given that the number of patients needed to be treated with corticosteroid prophylaxis to prevent one severe or fatal HSRs is high, questions arise about the risk-benefit ratio of prophylaxis in vulnerable patient populations. Not only is the need for timely diagnosis and treatment heightened, but extended hospitalization is recognized as a risk factor for hospital-acquired infection, morbidity, and mortality. The indirect costs and harms of premedication were examined in 2016 through a retrospective matched cohort study of 2,829 subjects: 1,424 were premedicated with the Greenberger regimen for a prior drug reaction, while 1,425 subjects were not premedicated. The authors demonstrated that premedicated subjects had significantly longer average times to procedure, significantly longer hospital stays, and significantly more hospital-acquired infections compared to control subjects who were not premedicated. Using these and other data in a hypothetical cohort analysis, the authors estimated that preventing one death related to HSR with hospital-based prophylaxis would cost \$131,211,400, extend hospital stays by a total of 162 years, contribute to 551 hospital-acquired infections, and lead to 32 deaths from infection. In a sensitivity analysis of the best-case scenario, where the greatest benefits of premedication were combined with the fewest harms, preventing one death due to a hypersensitivity reaction would still cost \$17,342,939, extend hospital stays by a total of 38 years, contribute to 55 hospital-acquired infections, and lead to 3 deaths from infection. In all tested scenarios in the sensitivity analysis, premedication in high-risk hospitalized patients led to more lives lost than saved. [21, 22]

The lack of established protocols for perioperative allergic reaction management in many countries highlights the need for appropriate strategies to identify at-risk patients and prevent recurrence. It is essential to involve both anesthesiologists and allergists in developing these protocols, and guidelines should be standardized across countries to ensure uniform management of perioperative HSRs.

The following prospective clinical trial aims to create an algorithm for perioperative care of patient with anamnesis of allergies.

MATERIALS AND METHODS:

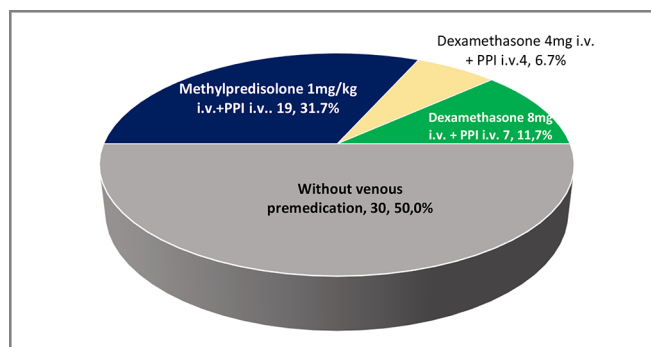
A prospective clinic-epidemiological study was conducted including 60 participants. A standardized approach to general anesthesia was used for all patients. After cannulating a peripheral venous cannula in the upper

limb, immediate premedication was administered, which included a proton pump inhibitor, Lidocaine 1% (1 mg/kg Adjusted Body Weight (ABW)), Midazolam 0.02-0.04 mg/kg Lean Body Weight (LBW), Fentanyl 0.05 mg intravenously, and preoxygenation for 3-5 minutes. Induction of anesthesia was performed with Propofol 2-2.5 mg/kg LBW and Suxamethonium 1-1.5 mg/kg Total Body Weight (TBW), followed by endotracheal intubation, which proceeded without complications in all 60 patients. Balanced anesthesia was maintained with the inhalation anesthetics Isoflurane for thyroid and parathyroid surgeries and Sevoflurane for adrenalectomies at the appropriate minimal alveolar concentrations in an oxygen/air mixture with a FiO₂ of 0.6 at a fresh gas flow. Intraoperative analgesia was achieved with fractionated administration of opioids—Fentanyl, dosed according to the pharmacokinetics and the patient’s clinical signs, such as changes in heart rate and blood pressure. Muscle relaxation was achieved with Atracurium at an initial dose of 0.5 mg/kg ABW. Standard intraoperative monitoring was performed on all patients. This included three-channel ECG monitoring with two leads (II and V5), non-invasive blood pressure measurement via oscillometry, pulse oximetry, capnography, the inspiratory and expiratory concentration of the inhalation anesthetic used, and oxygen. Postoperatively, following the recovery of consciousness, protective reflexes, and muscle strength after administration of Galantamine, patients were extubated and transferred for 24-hour observation in the postoperative intensive care unit. All patients received postoperative analgesia 30 minutes before the end of surgery and again in the evening using a combination of Tramadol 100 mg IV and Paracetamol 1.0 g/Ibuprofen 400 mg IV. With informed consent, patients were divided into two groups: “with” and “without” corticosteroid administration—Methylprednisolone 1 mg/kg/Dexamethasone 4/8mg. (Fig 1.). All patients reported a history of allergic reaction to one of the allergens listed in the inclusion criteria during the preoperative anesthetic consultation. Preoperative testing for reactions to drugs used during general anesthesia was conducted in thirty patients (50%). Randomly, intravenous corticosteroids (Methylprednisolone 1 mg/kg (19), Dexamethasone 8 mg IV (7), Dexamethasone 4 mg IV (4)) were administered as antiallergic premedication to 30 patients one hour before surgery. General anesthesia was conducted as described above. Signs of hypersensitivity and/or anaphylaxis, such as rash, soft tissue swelling, bronchospasm, and hypotension, were observed and documented intraoperatively and postoperatively at the 1st, 6th, 12th, and 24th hour. Additionally, blood glucose levels were measured, and pain was assessed using the Visual Analog Scale (VAS). If an allergic reaction occurred, the suspected allergen was discontinued, and adrenaline 0.3 mg IV was administered, along with boluses of water-electrolyte solutions for severe allergic reactions or anaphylactic shock, and bronchodilators were given for bronchospasm. The study results were documented in a work card containing the patient’s demographic data, type of surgical intervention,

allergy history, results from any testing (if applicable), the administered antiallergic premedication, and the observed and measured parameters

Data were entered and processed with the statistical packages IBM SPSS Statistics 27.0.1.0 and MedCalc Version 19.6.3. Microsoft Office Excel 2021 was also used for the figures. $p < 0.05$ was accepted as a level of significance at which the null hypothesis is rejected.

Fig. 1. Frequency distribution of patients by venous premedication.



The following methods were applied:

1. Descriptive analysis – the frequency distribution of the considered signs is presented in tabular form.
2. Analysis of variance – estimates of central tendency and statistical dispersion.
3. Graphical analysis – for visualization of the obtained results.
4. Fisher-Freeman-Halton exact test, Fisher’s exact test and χ^2 test - for testing hypotheses about the presence of dependence between categorical variables.

RESULTS:

Of 60 participants 12 (20.0%) were men and 48 (80.0%) were women in a ratio of 1:4. The average age of the studied contingent was 49.45 ± 13.39 years in the interval between 20 and 75. The terms of the frequency distribution of patients by type of operation is as follows With the largest relative share (70.0%) is Thyroidectomy, followed by Parathyroidectomy at 16.7%; With the smallest percentage (6.7% each) are Resectio glandulae thyroideae and other (REA – Retroperitoneal Endoscopic Adrenalectomy, Hemiglossectomia).

The results of the Table 1. Frequency distribution of comorbidities shows that of the accompanying diseases:

- With the largest relative share (16.7%) is diabetes mellitus, followed by bronchial asthma with 11.7%;
- With the smallest percentage (1.7) is atopic dermatitis;
- Most (66.7% or 2/3) are patients in the “Other” category, 16 or 26.7% have no accompanying diseases, and generally, for the studied sample their number is between 0 and 3 per patient.

Table 1. Frequency distribution of comorbidities shows that of the accompanying diseases.

	n	%	Sp
Other	40	66.7	6.1
None	16	26.7	5.7
Diabetes Mellitus	10	16.7	4.8
Bronchial Asthma	7	11.7	4.1
Hay Fever	4	6.7	3.2
Angioedema	3	5	2.8
Atopic Dermatitis	1	1.7	1.7
Total Number of Patients in Sample	60		

Note: The sum of percentages exceeds 100%, as some patients had more than one comorbidity.

Table 2 shows:

- After the leading group, “To other medications,” registered in 55.0% of patients, with the largest proportion of those with an allergy to NSAIDs at 15%, the largest relative share (31.7%) is allergies to antibiotics, followed by food allergies with 28.3%;
- Allergies related to “previous anesthesia” and hay fever have the lowest share (1.7% each).

Statistical analysis of the relationship between comorbidities and history of allergy did not reveal a significant correlation ($p=0.790$).

Table 2. Frequency distribution of allergy history shows that in terms of the frequency distribution of allergy history.

	N	%	Sp
To other medications	33	55	6.4
To antibiotics	19	31.7	6
To foods	17	28.3	5.8
To contrast agents	2	3.3	2.3
To latex	2	3.3	2.3
During previous anesthesia	1	1.7	1.7
Hay fever	1	1.7	1.7
Total Number of Patients in Sample	60		

Note: The sum of percentages exceeds 100%, as some patients had more than one comorbidity.

Half of the patients in the sample were not tested; Among patients undergoing testing, the largest relative proportion (35.0%) were patients testing positive for Nivalin/Lydol, followed by those testing positive for muscle relaxants (16.7%). (Table 3.) This relationship is expressed in statistically significant (or borderline significance $p<0.1$) higher relative shares of negative test results in patients with a history of allergy to antibiotics and foods, as well as in higher percentages of positive tests for Nivalin/Lydol in patients with a history of allergy to other

medications. The statistical analysis of the relationship between comorbidities and test results did not reveal a significant correlation ($p=0.778$).

Table 3. Frequency distribution of test results.

	n	%	Sp
No testing	30	50	6.5
Positive for Nivalin/Lydol	21	35	6.2
Positive for muscle relaxants	10	16.7	4.8
Positive for opioids	8	13.3	4.4
Negative tests	7	11.7	4.1
All positive	1	1.7	1.7
Total number of patients in sample	60		

Note: The sum of percentages exceeds 100%, as some patients had more than one comorbidity.

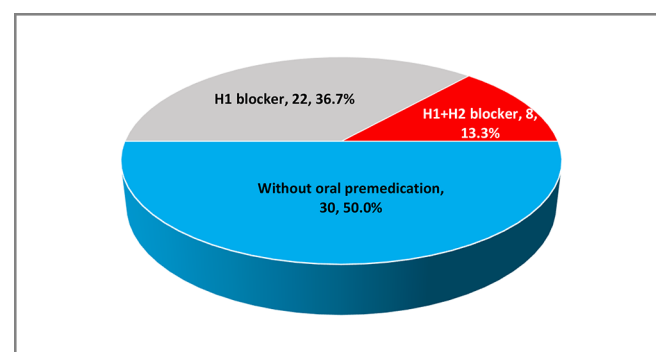
Regarding the frequency distribution of patients according to oral premedication (Fig. 2):

- The largest relative share (50.0%) was occupied by patients who did not receive premedication, followed by those who were administered an H1-blocker (36.7%);
- The lowest proportion (13.3%) was registered in patients who received combined premedication with H1 and H2-blocker.

The frequency distribution of patients regarding venous premedication:

- The largest relative share (50.0%) was occupied by patients who did not receive intravenous premedication, followed by those who received Methylprednisolone 1 mg/kg i.v. (31.7%);
- The lowest proportion (6.7%) was registered in the patients who received Dexamethasone 4 mg i.v.

Fig. 2. Frequency distribution of patients on oral premedication.



The results of Table 4. shows that 18 (30.0%) of patients had both types of premedication.

Regarding the frequency distribution of patients with intra- and postoperative rashes:

- Rash was observed only intraoperatively in two patients (3.3%);
- No rashes were registered in the remaining observation periods.

No edema occurred either during surgery or in the postoperative period.

Regarding the frequency distribution of patients with bronchospasm intra- and postoperatively:

- The complication occurred 1 hour and 6 hours after surgery, respectively, in two (3.3%) and one (1.7%) patients;
- No rashes were registered in all other observation periods.

The number of patients with rashes and bronchospasm is too small, which does not allow for conducting an analysis that would give statistically reliable conclusions.

Hypotension as a possible manifestation of HSRs in the intra- and postoperative period was not observed in any of the patients.

Table 4. Frequency distribution of patients by oral and intravenous premedication.

	Oral Premedication	Frequency		Total
		No	Yes	
No	n	18	12	30
	%	60	40	50
Yes	n	12	18	30
	%	40	60	50
Total	n	30	30	60
	%	100	100	100

DISCUSSION:

Allergic reactions, especially anaphylaxis during the perioperative period, represent a significant anesthesia-related complication, accounting for 5-7% of anesthesia-related deaths. During surgery, when patients are under anesthesia, early symptoms of severe allergic reactions—such as hoarseness, dizziness, difficulty swallowing, and speech issues—often go unnoticed. This lack of early warning signs and the potentially severe consequences highlight the need for specific protocols to prevent and manage allergic reactions. However, globally, and specifically in Bulgaria, such protocols are often the exception rather than the norm. Our study demonstrates that prior perioperative HSRs are a leading risk factor for allergic reactions or anaphylaxis in the perioperative period. These patients are five to six times more likely to experience a reaction than the general population, especially those who have previously had moderate (e.g., pronounced hives, mild bronchospasm, or facial/laryngeal edema) to severe reactions (e.g., hypotensive shock or respiratory/cardiac arrest). In one instance, a patient in our study had documented perioperative facial swelling during previous anesthesia. Furthermore, patients with conditions such as asthma, atopy, or hereditary/acquired angioedema are at particular risk. In our study, 25% of participants (15 patients) had atopic conditions, including bronchial asthma, hay fever, atopic dermatitis, and angioedema. Patients with a history of reactions to

NSAIDs, particularly cyclooxygenase-1 (COX-1) inhibitors, made up 15% (9 patients) of the study. Additionally, patients with allergies to latex and contrast agents accounted for 7% of the cases. Overall, nearly half (48%) of our patients fell into the high-risk category for perioperative HSRs. Other allergies reported included antibiotics, foods, antithyroid drugs, antihypertensives, dust, pollen, and insect allergens—all considered high-risk for perioperative HSRs in Bulgarian practice. Diagnosing and managing perioperative allergic reactions requires close collaboration between anesthesiologists and allergologists. Anesthesiologists handle the acute phase of the reaction, while allergologists focus on subsequent diagnostics to identify the causative allergen when possible. Skin testing remains the most effective method for determining whether a reaction is allergic or non-allergic in nature. Based on these results, recommendations can be made for future anesthetic procedures. For example, patients with a history of anaphylaxis or severe reactions during anesthesia should be referred to an allergologist to identify the triggering agent. According to the Spanish Society of Allergology and Clinical Immunology (SEAIC), preoperative testing should be reserved for patients with documented hypersensitivity during prior anesthesia. In our study, 50% of patients with a history of allergy underwent preoperative testing for anesthesia-related drugs. These patients were tested before admission, following referrals from other physicians. This included individuals with a history of allergies to household dust, pollen, food, and certain medications (e.g., beta-blockers and metformin). In 70% of those tested, positive results were obtained for Nivalin and Lydol—two drugs classified as histamine liberators. Despite these positive test results for Nivalin, the drug was administered at the end of anesthesia in all cases to reverse muscle relaxants. Only one patient exhibited an HSR (bronchospasm) postoperatively, who also had a history of allergic reactions during previous anesthesia and uncontrolled bronchial asthma, another risk factor. For 25% (7 patients), all test results were negative despite having a history of allergies to food, contrast agents, and antithyroid drugs. One patient had positive results for all tests and had a history of allergies to food and latex. For this patient, standard balanced anesthesia was performed after corticosteroid premedication. Although this patient experienced a transient intraoperative urticarial rash, no severe or delayed symptoms of anaphylaxis were observed. Interestingly, the correlation analysis showed that patients with atopic conditions did not have a higher rate of positive test results. In contrast, those with allergies to antibiotics and foods more frequently had negative results for all tested medications. Tests for Nivalin and Lydol were more commonly positive in patients with a history of allergies to other medications. Additionally, many patients self-reported allergy symptoms based on personal judgments of reactions to medications, such as redness, palpitations, nausea, or hot flashes. These symptoms, often linked to histamine release, explain the frequent positivity of tests for histamine-liberating drugs like Nivalin and Lydol.

However, these were more likely anaphylactoid rather than true allergic reactions and should not be treated as such. The results from this study emphasize the importance of clear documentation of patients' allergy histories to distinguish between allergic and anaphylactoid reactions. Due to the potential for inaccurate patient-reported information, medical professionals should interpret and document allergic or anaphylactic reactions. Preoperative testing should be reserved for patients with a history of HSRs during previous anesthesia or severe anaphylaxis of another origin. Testing does not benefit patients with atopy or food and latex allergies and can unnecessarily prolong the preoperative process, delaying surgery and consuming resources. It is important to note that positive test results do not necessarily indicate hypersensitivity to the tested medications. As confirmed in our study and the literature, preoperative testing has limited diagnostic value due to the varied mechanisms of HSRs. We recommend conducting preoperative testing only in patients with a history of hypersensitivity reactions during anesthesia or severe anaphylaxis from other causes. This practice aligns with international guidelines for preoperative preparation. Finally, our findings suggest that the routine use of corticosteroids or antihistamines as antiallergic premedication is not supported by clinical evidence. Although corticosteroids may help treat bronchospasm, they do not prevent HSRs. Therefore, their use as part of preoperative preparation in allergic patients should be reconsidered, and alternative strategies should be explored. One possible strategy, suggested by several guidelines, including from the NAP6 project, recommends intravenous administration of antibiotics before anesthesia induction to avoid the combination of anesthesia induction and antibiotic administration. Following the results from the study, we suggest that the most reliable method to prevent perioperative HSRs is to avoid the drugs identified as trigger of previous HSRs.

One of the limitations of the study is the small number of patients with a history of latex allergies. Therefore, our recommendation to exclude these patients from the high-risk group is of low reliability and requires further, larger-scale research. The lack of a standardized approach to preoperative testing and the administration of oral premedication could also be interpreted as a limitation of the study. Another limitation is the small number of patients who developed perioperative HSRs, which does not allow for the extraction of statistically significant dependencies. However, this outcome supports the hypothesis of overdiagnosis of allergic reactions and the unnecessary execution of preoperative preparation. In light of the data presented in the literature review and our study, and drawing from the positive experience of countries with established protocols and collaboration between responsible specialists, we recommend the development of a national protocol for managing perioperative hypersensitivity reactions in collaboration with allergologists.

CONCLUSIONS:

Based on the literature review and the analysis of the results from our study on the effectiveness of prick test and corticosteroids/antihistamines as antiallergic premedication, the following conclusions can be drawn:

- There is no standardized protocol for diagnosing, preventing, and treating of HSRs in the perioperative period in Bulgaria.
- A detailed allergy history should be obtained to clarify the specific circumstances and symptoms of previous allergic reactions. It is recommended that the allergy history be taken from the accompanying medical documentation.
- Preoperative testing for drugs used during anesthesia should only be conducted in patients with a history of allergic reactions during previous anesthesia and/or anaphylaxis under other circumstances.
- Preoperative testing is not justified in patients with atopic conditions or a history of allergies to foods, latex, insects, pollen, dust, and other medications unless associated with the development of anaphylaxis.
- The analysis of preoperative test results should be interpreted in the context of the clinical situation, particularly regarding the patient's susceptibility to histamine release.
- The absence of corticosteroid prophylaxis does not lead to an increase in the occurrence of perioperative HSRs.
- The administration of corticosteroid premedication does not prevent either mild or moderate-to-severe HSRs, nor does it prevent early or late HSRs.
- The absence of H1 +/- H2 blockers in the premedication does not increase the incidence of perioperative HSRs.
- The administration of H1 +/- H2 blockers does not prevent either mild or moderate-to-severe HSRs, nor does it prevent early or late HSRs.

Abbreviations:

- ABW - Adjusted Body Weight
- AR - Adverse reaction
- CS - Corticosteroid
- HSR - Hypersensitivity reactions
- LBW – Lean Body Weight
- NSAID – Non-steroidal anti-inflammatory drug
- REA – Retroperitoneal Endoscopic Adrenalectomy
- SEAIAC - Spanish Society of Allergology and Clinical Immunology
- TBW – Total Body Weight
- VAS - Visual Analog Scale

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