SHORT COMMUNICATION

Quality, safety and efficacy in a communication protocol between the anesthesiologist and the allergist in perioperative hypersensitivity reactions

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Received 18 June 2021; accepted 24 October 2021
Available online 16 December 2021

Suspected hypersensitivity reactions in the perioperative period are unpredictable critical events with a potential risk of morbidity, such as neurological damage and mortality.1 They pose a major challenge due to the various substances administered consecutively, hidden exposures, and associated clinical conditions that can make the clinical presentation difficult to recognize. Other clinical scenarios can mimic the presentation of hypersensitivity, whose confirmation is essential for safety in future exposures,2 since it is impossible to determine clinically whether the reaction is immunological or not.3 Correct investigation should guide appropriate management of future exposure of a patient.

Anesthesiologists are the professionals who most frequently witness hypersensitivity reactions during the perioperative period, diagnosing and treating the events, as well as collecting blood samples to measure mediators for diagnosis.

The interaction among anesthesiologists, allergists and immunologists, among others with extensive knowledge in drug allergy and perioperative anaphylaxis,4 is warranted to identify triggering agents as well as the reaction mechanism, in order to reduce the occurrence of re-exposure to triggering agents and, consequently, reduce morbidity and mortality, and prevent perioperative anaphylaxis.

As in other organizations, the use of appropriate terminology among the teams involved is essential for successful management. Using a standardized vocabulary allows standardizing the data to be studied and minimizing missing information.

Thus, the proposal for a standardized instrument is presented in order to facilitate reporting of suspected perioperative allergy reactions, simplify communication among the professionals involved, help plan actions for diagnosis and guidance, and collect data for epidemiological studies.

An instrument for investigating perioperative hypersensitivity reaction was standardized (Fig. 1). The instrument consists of patient identification, admission data, place and time of reaction, substances used, description of the reaction, management of the reaction, outcome of the procedure, and test and investigation results.

The term hypersensitivity is comprehensive, as it encompasses reactions whose underlying mechanism may be allergic or non-allergic. It should be used to objectively describe reproducible symptoms or signs initiated by exposure to a defined stimulus at a dose tolerated by normal individuals.3 This, therefore, is the appropriate term to describe a

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https://doi.org/10.1016/j.bjane.2021.10.016
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suspected clinical manifestation until the mechanism involved in the reaction is elucidated. The World Allergy Organization (WAO), responsible for the revision of allergy nomenclature for global use, has recommended the standardization of terms.

In convergence with the importance of nomenclature and correct classification of hypersensitivity events, not restricted to the perioperative period, the World Health Organization (WHO) introduced the subsection on hypersensitivity to drugs, in its International Classification of Diseases, WHO ICD-11, aiming at more accuracy in the registration of events and collection of epidemiological data, which support better quality care and action planning.

According to the current nomenclature, allergy is any hypersensitivity reaction triggered by a specific immune mechanism. Anaphylaxis, in turn, is defined as immediate onset of a systemic reaction, with life-threatening respiratory and circulatory impairment. There is also non-allergic hypersensitivity, which defines the clinical presentation resulting from non-specific (direct) activation of cells of the immune system. The modified Ring and Messmer scale is used to classify perioperative reactions clinically, according to the degree of intensity.

In the investigation process of a perioperative reaction suspected of allergy, standardization in reporting can help minimize the risk of incomplete information and simplify communication among the professionals involved, helping to plan actions toward the correct diagnosis.

In a series of seventy patients assessed for perioperative hypersensitivity reaction, three of them had a new reaction on a subsequent exposure. In two of them, partial or
incomplete information was the cause of inadvertent re-
exposure to the causative agent; in the third, the cause was
mastocytosis.1

In the investigation of suspected allergic reactions, an
emerging challenge is the search for hidden agents adminis-
tered by other routes of exposure that are not as clear. Anti-
biotics delivered by bone cement or surgical cement,
methylene blue added to blood derivatives for viral inactiva-
tion are a few mentioned.7 Recently, polyethylene glycols,
which are widely used as excipients in medicinal products,
including sprays of local anesthetics, cosmetics, and house-
hold products, have been implicated as a suspected cause of
anaphylaxis after the application of the mRNA COVID-19 vac-
cine.8 Other possible agents rarely considered and that
should deserve attention in the investigation are biological
glues, hemostatic agents, irrigation fluids applied to the
operative site, in addition to drug excipients and
disinfectants.7

The less comprehensive version of the standardized
instrument for investigating perioperative hypersensitiv-
ity reaction was presented at the World Allergy Confer-
ence.9 It is a clinical practice-related protocol of the
Núcleo de Avaliação de Reações do Tipo Alérgico a Dro-
gas (NARTAD), in compliance with the recommendations
established by services specializing in perioperative
allergy investigation.4 It corresponds to the norms
established by the Núcleo, performing in vivo tests with
neuromuscular blockers, antibiotics, opioids, Non-Steo-
r oid Analgesics (NSA), local anesthetics, latex and chlor-
hexidine. Skin tests are performed by prick test, and
are intradermal; if indicated, challenge tests are also
used. In vitro tests, such as specific measurement of

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**Figure 1 Continued.**

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V – Reaction data:
Was there a time relationship between exposure to any
substance and symptom/sign onset?
☐ Yes Describe: ____________________________
☐ No

Time surgery initiated: __________________________

Time reaction initiated: __________________________

Signs and symptoms observed (List in chronological order):
- Erythema
- Pruritus
- Urticaria
- Angioedema
- Airway pressure increase
- Bronchospasm
- Cyanosis/Desaturation (minimum saturation value %)
- Tachycardia
- Bradycardia
- Anuria
- Hypotension (minimum value observed, mmHg)
- Cardiopulmonary arrest

Others: __________________________

According to the classification, what is the level of
severity of the reaction presented by the patient?
Modified Ring-Messer classification² (Severity Scale for
Immediate Hypersensitivity Reactions):

☐ Grade I – Skin symptoms: Generalized erythema,
urticaria, angioedema

☐ Grade II – Detectable symptoms but not life-
threatening: skin signs, hypotension, tachycardia,
cough, breathing difficulties

☐ Grade III – Life-threatening symptoms: cardio-
vascular collapse, tachycardia or bradycardia, anuria,
bronchospasm

☐ Grade IV – Cardiopulmonary arrest

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VI – Reaction management:
Treatment provided (by chronological order):
☐ Trendelenburg Position
☐ IV Fluids
☐ Oxygen
☐ ETT required
☐ Airway intubated
☐ Mask
☐ Epinephrine

Route: ____________________________
Dose: ____________________________
Vasopressor? Specify: ____________________________

☐ Glucagon
☐ Corticoids
☐ Anti-histaminic
☐ Others: ____________________________

Blood sample to determine tryptase:
☐ up to 2 hours after reaction
☐ 2–4 hours after
☐ 24 hours
☐ Not performed

VII Procedure outcome
☐ Abbreviated surgery
☐ Surgery concluded as scheduled
☐ Surgery cancelled for:

Patient follow up / recovery at:
☐ SRPA
☐ Inpatient Unit
☐ ICU: ☐ Ventilatory Support
☐ Vasodepressor drugs

Inpatient Stay:
☐ Unit days:
☐ ICU days:

☐ Deceased
Time of occurrence:
☐ During treatment of reaction
☐ Up to 24 h after reaction
☐ 24–48 h after reaction
☐ 48 h after reaction

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IgE, tryptase, may also be requested as part of the investigation.

Anesthesiologists and allergists participated in the definition of information used to standardize perioperative hypersensitivity tests. The resulting final adjustments are presented in Figure 1.

The presentation of the instrument aims toward ample promotion and use among professionals involved in the investigation of suspected perioperative allergy events. Similar instruments are also used in other countries.10

Questions originated from the previously published standardized instrument9 allowed the development of two questionnaires aimed at mapping events, their characteristics and diagnostic and therapeutic measures adopted. One questionnaire was distributed to Allergy specialists and another to Anesthesiology specialists, and answers are still to be evaluated. A third, more comprehensive and multicentric study, along with a national research network in Anesthesiology, is being prepared, and data collecting is anticipated for next year.

The communication protocol is expected to become simpler in order to report and send suspected perioperative hypersensitivity reactions for investigation, and, thus, move in the direction of the more widely recommended objective of preventing the risk event to occur. Moreover, “we aim to promote a warning sign related to anaphylaxis and strengthen patient safety culture”.

Finally, we understand that employing a communication instrument between anesthesiologists and allergists to

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### Figure 1 Continued.

| Questionnaire | Yes | No |
|---------------|-----|----|
| IgE-dependent reaction identified? | ☐ | ☐ |

Final Diagnosis:

- Drugs to be avoided until further investigation:

- Drugs to be absolutely avoided:

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**Obs:** In case of tests positive to Neuramalicular Blockers (NMB), use only agents with negative result tests. New NMB introduced into practice, should be tested before using, due to high MB cross-reactivity.

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**Legend:**

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- **(AIO):** American Society of Anesthesiologists
- **(P):** Physical Status (American Society of Anesthesiologists)
- **(PMA):** Patient Management Assessment
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**Figures:**

- **Figure 1 Continued.**

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**Table:**

| Questionnaire | Yes | No |
|---------------|-----|----|
| IgE-dependent reaction identified? | ☐ | ☐ |

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**Questions:***

- **Was an IgE-dependent reaction identified?**
  - Yes
  - No

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**Final Diagnosis:**

- Drugs to be avoided until further investigation:

- Drugs to be absolutely avoided:

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**Figures:**

- **Figure 1 Continued.**
assess suspected perioperative or periprocedural hypersensitivity reactions during a period is a major step, in the cumbersome process of acknowledging, treating, diagnosing and preventing future reactions.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgements

We thank our colleague anesthesiologists and allergists who contributed with their reviews and suggestions to improve the present protocol.

References

1. Miller J, Clough SB, Pollard RC, Misbah SA. Outcomes of repeat anesthesia after investigation for perioperative allergy. Br J Anaesth. 2018;120:1195–201.
2. Melchior BLB, Garvey LH. Investigation of perioperative hypersensitivity reactions: an update. Curr Opin Allergy Clin Immunol. 2020;20:338–45.
3. Garvey LH, Ebo DG, Mertes PM, et al. An EAACI position paper on the investigation of perioperative immediate hypersensitivity reactions. Allergy. 2019;74:1872–84.
4. Egner W, Cook T, Harper N, et al. Specialist perioperative allergy clinic services in the UK 2016: results from the Royal College of Anaesthetists Sixth National Audit Project. Clin Exp Allergy. 2017;47:1318–30.
5. Johansson SG, Bieber T, Dahl R, et al. Revised nomenclature for allergy allergy for global use: report of the nomenclature committee of the world allergy organization, October 2003. J Allergy Clin Immunol. 2004;113:832–6.
6. Tanno LK, Bierrenbach AL, Simons FER, et al. Critical view of anaphylaxis epidemiology: open questions and new perspectives. Allergy Asthma Clin Immunol. 2018;14:12.
7. Old Garvey LH. New and hidden causes of perioperative hypersensitivity. Curr Pharm Des. 2016;22:6814–24.
8. Garvey LH, Nasser S. Anaphylaxis to the first COVID-19 vaccine: is polyethylene glycol (PEG) the culprit? Br J Anaesth. 2021;126:e106–8.
9. Spindola MA, Da Silva J, Morato EF. Evaluation of perioperative hypersensitivity reactions: post-event interaction between anesthesiologist and allergist. World Allergy Organ J. 2015;8(1): A143.. Suppl.
10. Laguna JJ, Archilla J, Doña I, et al. Practical guidelines for perioperative hypersensitivity reactions. J Investig Allergol Clin Immunol. 2018;28:216–32.