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SHORT COMMUNICATION

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

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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, reaction management, 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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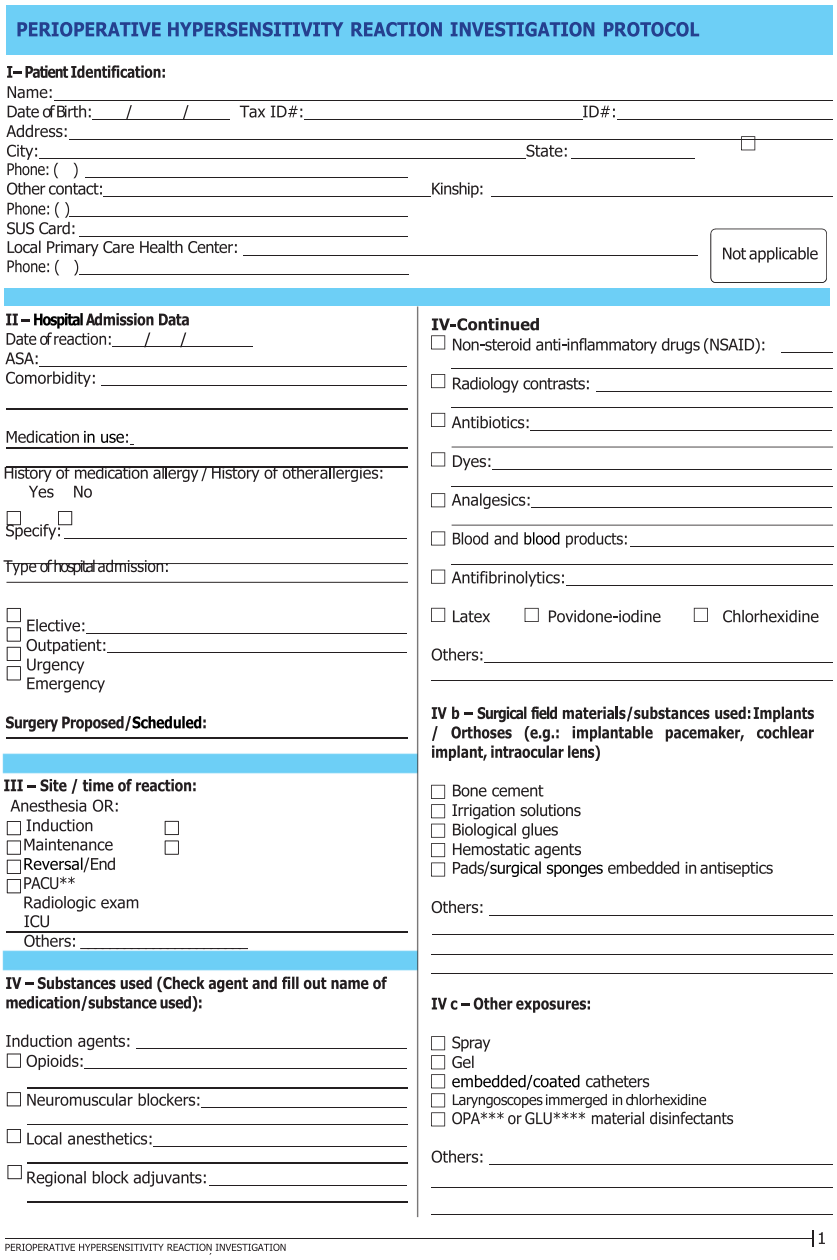


PERIOPERATIVE HYPERSENSITIVITY REACTION INVESTIGATION PROTOCOL

I– Patient Identification:
Name:
Date of Birth: / / Tax ID#: ID#:
Address:
City: State:
Phone: ( )
Other contact: Kinship:
Phone: ( )
SUS Card:
Local Primary Care Health Center:
Phone: ( )
Not applicable

II – Hospital Admission Data
Date of reaction: / /
ASA:
Comorbidity:
Medication in use:
History of medication allergy / History of other allergies:
Yes No
Specify:
Type of hospital admission:
Elective:
Outpatient:
Urgency
Emergency
Surgery Proposed/Scheduled:

III – Site / time of reaction:
Anesthesia OR:
Induction
Maintenance
Reversal/End
PACU**
Radiologic exam
ICU
Others:

IV – Substances used (Check agent and fill out name of medication/substance used):
Induction agents:
Opioids:
Neuromuscular blockers:
Local anesthetics:
Regional block adjuvants:

IV-Continued
Non-steroid anti-inflammatory drugs (NSAID):
Radiology contrasts:
Antibiotics:
Dyes:
Analgesics:
Blood and blood products:
Antifibrinolytics:
Latex Povidone-iodine Chlorhexidine
Others:

IV b – Surgical field materials/substances used: Implants / Orthoses (e.g.: implantable pacemaker, cochlear implant, intraocular lens)
Bone cement
Irrigation solutions
Biological glues
Hemostatic agents
Pads/surgical sponges embedded in antiseptics
Others:

IV c – Other exposures:
Spray
Gel
embedded/coated catheters
Laryngoscopes immerged in chlorhexidine
OPA*** or GLU**** material disinfectants
Others:

PERIOPERATIVE HYPERSENSITIVITY REACTION INVESTIGATION 1

Figure 1 Perioperative or periprocedural hypersensitivity reaction post-reaction assessment protocol.

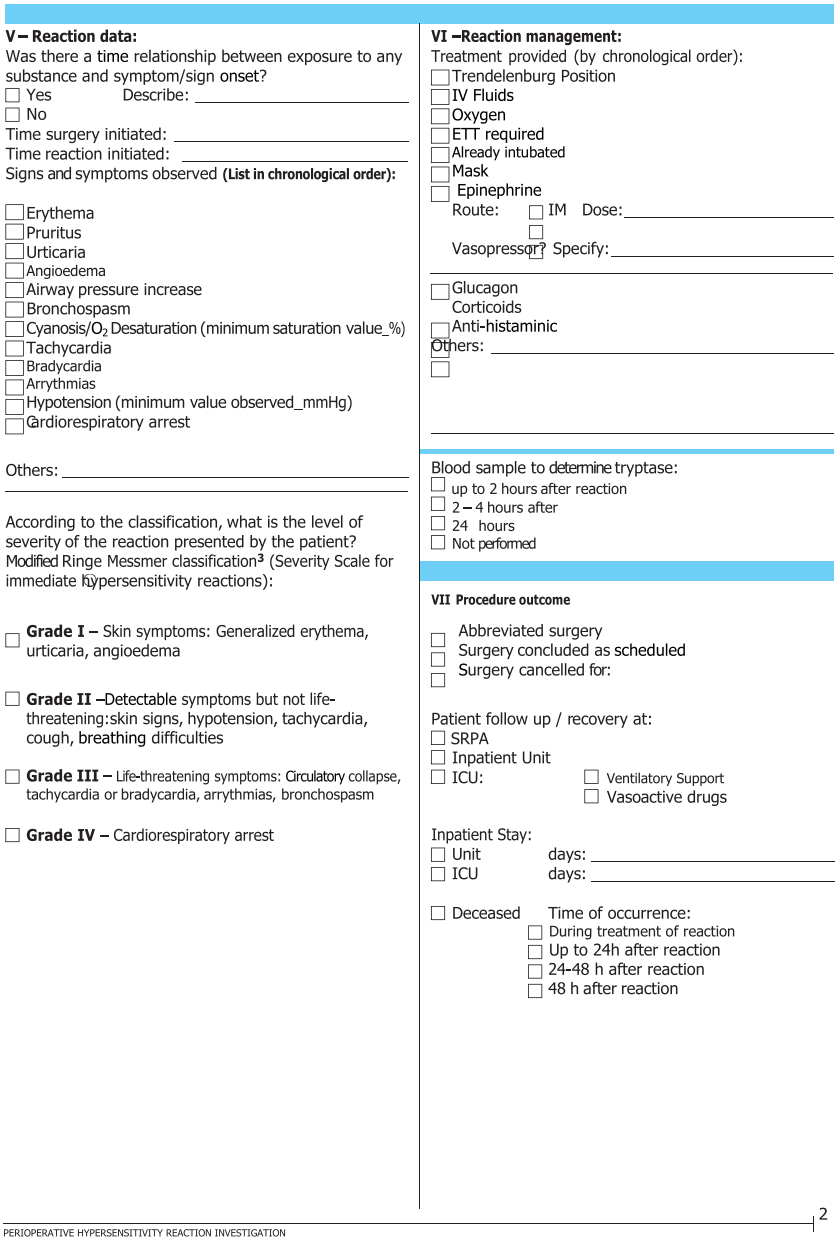
suspected clinical manifestation until the mechanism involved in the reaction is elucidated.[3] The World Allergy Organization (WAO), responsible for the revision of allergy nomenclature for global use, has recommended the standardization of terms.[5]

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.[6]

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.[5] The modified Ring and Messmer scale is used to classify perioperative reactions clinically, according to the degree of intensity.[3]

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



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/O_2 Desaturation (minimum saturation value_%)
☐ Tachycardia
☐ Bradycardia
☐ Arrythmias
☐ Hypotension (minimum value observed_mmHg)
☐ Cardiorespiratory arrest

Others: _____

According to the classification, what is the level of severity of the reaction presented by the patient? Modified Ringe Messmer classification[3] (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: Circulatory collapse, tachycardia or bradycardia, arrythmias, bronchospasm

☐ **Grade IV –** Cardiorespiratory arrest

VI –Reaction management:
Treatment provided (by chronological order):
☐ Trendelenburg Position
☐ IV Fluids
☐ Oxygen
☐ ETT required
☐ Already intubated
☐ Mask
☐ Epinephrine
Route: ☐ IM 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 ☐ Vasoactive drugs

Inpatient Stay:
☐ Unit days: _____
☐ ICU days: _____

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

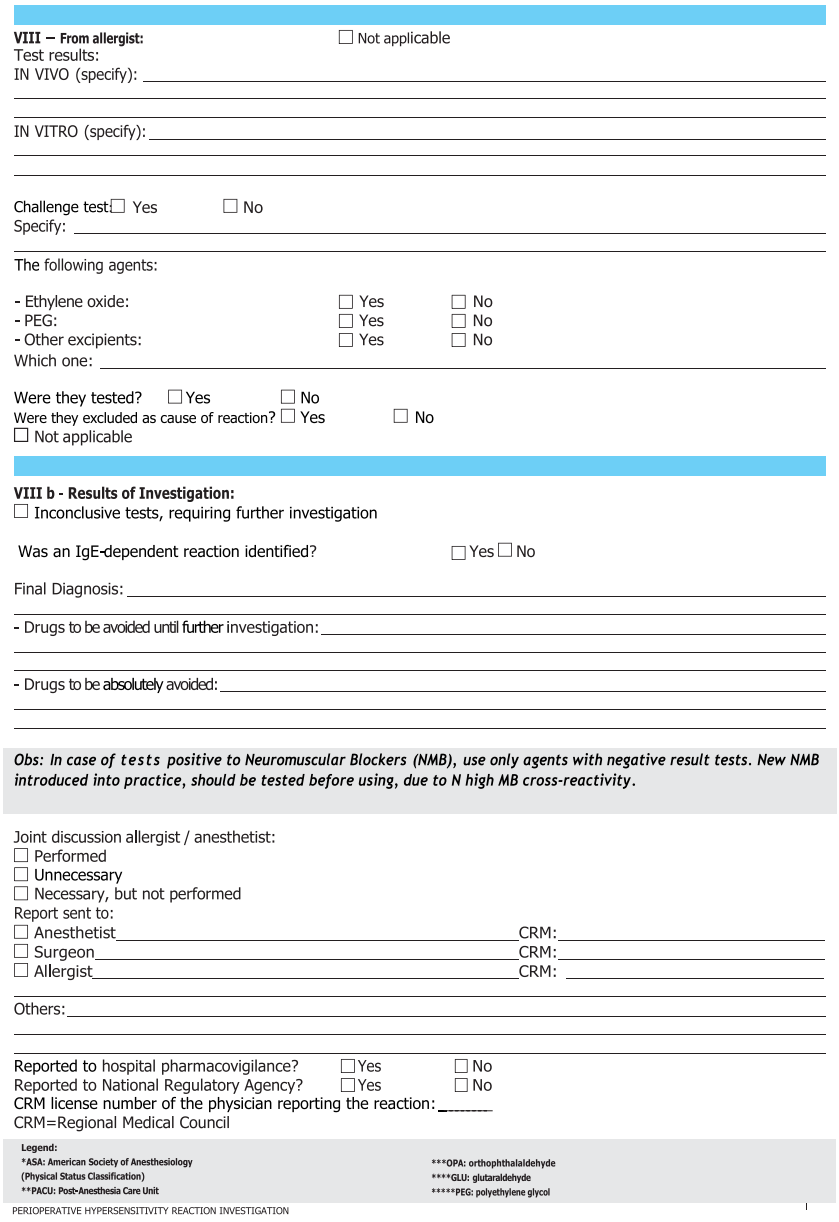
PERIOPERATIVE HYPERSENSITIVITY REACTION INVESTIGATION 2

Figure 1 Continued.

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 administered by other routes of exposure that are not as clear. Antibiotics delivered by bone cement or surgical cement, methylene blue added to blood derivatives for viral inactivation are a few mentioned.[7] Recently, polyethylene glycols, which are widely used as excipients in medicinal products, including sprays of local anesthetics, cosmetics, and household products, have been implicated as a suspected cause of anaphylaxis after the application of the mRNA COVID-19 vaccine.[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 hypersensitivity reaction was presented at the World Allergy Conference.[9] It is a clinical practice-related protocol of the Núcleo de Avaliação de Reações do Tipo Alérgico a Drogas (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-Steroid Analgesics (NSA), local anesthetics, latex and chlorhexidine. 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



VIII – From allergist: ☐ Not applicable
Test results:
IN VIVO (specify): _____

IN VITRO (specify): _____

Challenge test: ☐ Yes ☐ No
Specify: _____

The following agents:

- Ethylene oxide: ☐ Yes ☐ No
- PEG: ☐ Yes ☐ No
- Other excipients: ☐ Yes ☐ No

Which one: _____

Were they tested? ☐ Yes ☐ No
Were they excluded as cause of reaction? ☐ Yes ☐ No
☐ Not applicable

VIII b - Results of Investigation:
☐ Inconclusive tests, requiring further investigation

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

Final Diagnosis: _____

- Drugs to be avoided until further investigation: _____

- Drugs to be absolutely avoided: _____

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

Joint discussion allergist / anesthetist:
☐ Performed
☐ Unnecessary
☐ Necessary, but not performed

Report sent to:
☐ Anesthetist _____ CRM: _____
☐ Surgeon _____ CRM: _____
☐ Allergist _____ CRM: _____

Others: _____

Reported to hospital pharmacovigilance? ☐ Yes ☐ No
Reported to National Regulatory Agency? ☐ Yes ☐ No
CRM license number of the physician reporting the reaction: _____
CRM=Regional Medical Council

Legend:
*ASA: American Society of Anesthesiology (Physical Status Classification)
**PACU: Post-Anesthesia Care Unit
***OPA: orthophthalaldehyde
****GLU: glutaraldehyde
*****PEG: polyethylene glycol

PERIOPERATIVE HYPERSENSITIVITY REACTION INVESTIGATION

Figure 1 Continued.

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 instrument[9] 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

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.

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