Research Paper Medicine

Allergic Reactions to Local Anesthetics in Clinical Practice

Polliana Mihaela Leru	Carol Davila University of Medicine and Pharmacy, Faculty of Medicine, Bucharest, Romania
Dumitru Matei	Carol Davila University of Medicine and Pharmacy, Faculty of Medicine , Bucharest, Romania
Camelia Ionescu	Carol Davila University of Medicine and Pharmacy, Faculty of Dental Medicine, Romania

ABSTRACT

In the light of increasing burden of allergic diseases, drug allergies represent an important problem in clinical practice, with still many unclear aspects. Local anesthetics are drugs largely used in dental clinical practice, oro-facial surgery, as well as dermatology and other superficial interventions. Their current use may be associated with risks of adverse reactions in selected patients, some of them being allergies, with consequences that should be evaluated by an interdisciplinary approach. Local anesthetic medicines are generally well tolerated, but adverse reactions either allergic or non-allergic may occur and give rise to problematic situations for patients and doctors. It is recommended that all specialists using local anesthetics, as well as family doctors be aware about the real risk of these drugs, in order to avoid either more severe reactions or overestimation of their side effects.

KEYWORDS allergic reactions, clinical practice, local anestheticss

Introduction

Allergic diseases represent a pathology with a continuously increasing prevalence, being considered a real epidemic of the XXI century. It is estimated that during less than 20 years almost half of the population will suffer from a certain form of allergy and the causes of this epidemiologic trend are not completely understood. Drug allergies are hypersensitivity reactions (DHRs) induced by medicines, with an immunologically–mediated mechanism, representing 15% of all adverse drug reactions (1). Their actual incidence varies from 7% to 10% of the general population and has an increasing trend, with still many unclear aspects in terms of mechanisms, clinical pattern and diagnosis (1).

The rapid development of new drugs to treat or diagnose human illness has the consequence of an increased incidence of adverse reactions to these agents, producing additional morbidity and mortality. Most adverse reactions are not severe, but predictability of severity may be not possible in individual cases or for individual drugs and additional risk factors should be taken into consideration(2).On the other hand doctors should not deprive patients of necessary medication or intervention for fear of an adverse reaction. In order to avoid diagnostic confusion and therapeutic errors, the definition and classification of adverse drug reactions should be clear and uniform for all practitioners .

Definition and classification of adverse drug reactions

An adverse drug reaction may be defined as a response to a medicinal product which is noxious and unintended (Art.1/11, Directive 2001/83/EC, as amended). The reaction should appear within a reasonable time after administration of the drug. Adverse drug reactions may mimic virtually every disease, including the disease being treated! The challenge of monitoring adverse drug reactions is further complicated by multiple drug prescribing and the frequent use of non-prescription medications. Between 15% and 30 % of hospitalized patients experience an adverse drug reaction, but most adverse drug reactions do not have an allergic basis (3). The presence or absence of allergy to a certain drug may be imperative to establish in some patients , when its use is absolutely necessary and there is no safe alternative. Although many patients with a history of reacting to a drug could safely receive that drug again, the outcome could be serious if that patient is really allergic, therefore the suspicion of drug allergy must be evaluated carefully. Adverse drug reactions may be divided in two major groups: 1.predictable adverse reactions (type A), that account for more than 80%, are often dose-dependent and related to the known pharmacologic actions of the drug (overdosage, side effects, disease–asociated and drug-drug interactions) and 2. unpredictable adverse reactions, that are usually dose-independent, unrelated to the pharmacologic actions and occur in susceptible patients only. The unpredictable adverse drug reactions are: intolerance, idiosyncratic, allergic (hypersensitivity) and pseudoallergic reactions (4).

Drug hypersensitivity reactions (DHRs) are adverse effects of drugs that clinically resemble allergic reactions and can be allergic or non-allergic. Drug allergies are DHRs for which a definite immunologic mechanism is demonstrated and this term is recommended for general communication whenever a drug reaction is suspected. Drug allergies are typically unpredictable, necessitate treatment changes and can be potentially life-threatening. A definite diagnosis of drug allergy, enabling the institution of adequate treatment and proper preventive measures requires a complete allergy work-up, performed by a trained specialist. Several guidelines and consensus statements on general or specific drug class–induced DHRs are available to support medical decisions on drug allergy. Doctors and patients should know that there are no standardized protocols and systematic approach for the diagnosis and management of DHRs induced by all potential drugs and are still unmet needs in this pathology field. The International Collaboration in Asthma, Allergy and Immunology (ICAALL) formed in 2012 by some of the most prestigious allergy organizations has recently issued the International Consensus (ICON) on Drug Allergy document, with the aim of providing a concise reference in this pathology (1).

Evaluation of allergic reactions to local anesthetics

Local anesthetics are drugs largely used in dental clinical prac-

tice, oro-facial surgery, as well as dermatology and other superficial interventions.

Local anesthetics medicines are generally well tolerated, but adverse reactions either allergic or non-allergic may occur and give rise to problematic situations for patients and doctors. It is recommended that all specialists using local anesthetics, as well as family doctors be knowledgeable about the real risk of these drugs, in order to avoid either more severe reactions or overestimation of their side effects.

Local anesthetics are structurally classified as either ester or amide compounds. Esters, as derivatives of para-aminobenzoic acid, include: cocaine, procaine, tetracaine, benzocaine and cloroprocaine. They are associated with a higher incidence of allergic reactions and are actually much less used in clinical practice. Amides are most widely used today and include lidocaine, mepivacaine, prilocaine, bupivacaine, dibucaine, articaine (5)

Local anesthetics are compounds that block the sensory impulse traffic along the nerves. Their clinical effects depend on their ability to diffuse across nerve cell membranes and to bind sodium ion channels blocking sodium influx and nerve depolarization(6).The pharmacokinetics of local anesthetics refers to three factors: potency, onset of action and duration of blockade. Anesthetic potency is correlated with the lipophylicity of the substance, while the onset of action is dependent to the dose of the agent. The duration of action is dependent upon protein binding and the degree of vasodilatation induced, which results in elimination of the local anesthetic from the site of action. Short acting agents (procaine, clorprocaine) are preferred when a short duration of action is needed (15-30 minutes), but for longer procedures (60-90 min) agents like lidocaine, mepivacaine and prilocaine are better (6).

Practical aspects during local anesthesia

The most frequently used local anesthetics in clinical practice are: lidocaine 1% or 2% for troncular anesthesia, mepivacaine, which is better tolerated and has also vaconstrictor action due to its pyridinic ring, bupivacaine, prilocaine. Other medicines contain a fixed dose combination of anesthetic substance plus vasoconstrictors like adrenaline, in order to obtain increased efficacy and reduced toxicity and allergenic risk, for example Ubistesin (articaine plus adrenaline), mepivacaine plus levonordefrine (7).The incidence of adverse reactions induced by local anesthetics is generally low, about 2-3 % of all local anesthesia cases. The true incidence of allergic reactions is not known, being considered less than 1% of all anesthetic-induced reactions (8). The evaluation of possible allergic reactions induced by local anesthetics, as all other drug allergies, should first take into consideration drug and treatment related risk factors and patient-related risk factors. The drug–related risk factors are: the nature of the substance, dose, duration and frequency of administration. The patient-related risk factors are: age, gender, genetic factors (atopy, acetylator status, familial drug allergy), prior drug reactions (cross sensitization, multiple drug allergy syndrome), concurrent medical illness (asthma, cardiac diseases, viral infections, immunodeficiencies), concurrent medications (e.g. betablockers). Patient history is the most important for identification of risk factors and it should be taken carefully before any procedure involving local anesthesia. Dentists or other specialists using local anesthetics should be aware of the real risk of these drugs and refer to specialists only those patients with relevant risk factors or after circumstances evocative for possible allergic reactions. Patients who experience adverse reactions of virtually any type following the injection of a local anesthetic may be advised erroneously that they are allergic to these agents and may be denied the benefit of dental care or a surgical procedure. The patient considering himself allergic to many drugs or other substances, but not confirmed by specialist is a frequent situation encountered in clinical practice, that need careful evaluation and may be frustrating for both doctors and patients.

Differential diagnosis of allergic reactions during local anesthesia

Most of the adverse reactions occurring during local anesthesia are not induced by local anesthetics and may be: vaso-vagal reactions, hyperventilation, adrenergic reactions, operative trauma, epinephrine side effects, psychogenic or toxic reactions. Other reactions are usually due to an inadvertent rapid intravascular injection or extravascular administration of an excessive amount of a local anesthetic substance (9).The toxic reactions in normal subjects are very rare, consisting in: dysrhythmias, cardiovascular collapse, central nervous system effects, transient neuropathic symptoms. Overdose is not common in dental practice, but can occur and exceptionally can be fatal. The central nervous system is more susceptible to the toxic effects (9).Other reactions may be induced by adjuvants, like parabens and sulphites used as preservatives in local anesthetics or by epinephrine, antibiotics or analgesics (10). Another substance to be considered in case of a possible reaction during local anesthesia is latex, contained by gloves or other rubber products used in dental and surgical practices. Local or systemic reactions may occur in latex-sensitive patients and this possibility should be considered in the differential diagnosis of adverse reactions attributed to local anesthetic (11). Clinical forms of allergic reactions to local anesthetics can be immediate, like urticaria, angioedema and anaphylaxia (exceptionally) or delayed (type IV hypersensitivity reaction), such as allergic contact dermatitis, which is the most common immunologic reaction to local anesthetics. Other possible cutaneous reactions are localized eczema, at the site of application or more disseminated form, as hand dermatitis in exposed professionals, more rarely delayed edema. An important aspect in clinical practice is cross-reactivity between different local anesthetics, which is more frequent with esters, but unusual with amides(9).

Allergologic investigation of allergic reactions to local anesthetics

Evaluation of possible allergic reactions induced by local anesthetics should be performed by a specialist in allergology and clinical immunology, with specific training to recognize and treat the reaction, to identify relevant risk factors and indicate adequate investigations. The preferred investigation methods are in vivo, represented by skin tests. These are prick tests and intradermal tests for immediate reactions and patch tests for delayed –type reactions. Skin tests can be performed with commercial available local anesthetics without adrenaline (9). In vitro tests like measurements of specific IgE to local anesthetics or basophil-degranulation tests have limited diagnostic value, but may be sometimes used as initial diagnostic method in cases of patients at risk. Their interpretation should be done cautiously and correlated with clinical data. Challenge skin test may be performed with local anesthetics containing adrenaline. Most of the allergists recommend that pacients with atopy, relevant history of drug allergy or previous reactions to local anesthetics be evaluated under close monitoring (12).

Conclusions

Allergic reactions to local anesthetics may be problematic in clinical practice for dental specialists, surgeons, dermatologists, family doctors and other physicians, in case of selected patients, who need an interdisciplinary approach. Even though local anesthetics are generally well tolerated, some severe reactions may occur, depending on drug and patient risk factors. The advise of a specialist in allergology and clinical immunology is important and should be asked before intervention in all patients who have experienced a potentially allergic reaction during a local anesthesia. Allergy evaluation is complex, it involves detailed history, differential diagnostic, in vitro and in vivo tests and requires medical skills and careful monitoring.

Conflicts of interest :

the authors declare that they have no conflicts of interest in relation with this paper

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