



## **Allergic Reaction of the Body to Drugs Used in Dental Practice**

**Anastasiia Vladimirovna Shefova<sup>1\*</sup>, Andrey Olegovich Galustyan<sup>2</sup>,  
Angelina Olegovna Shershneva<sup>3</sup>, Olga Vladimirovna Tyukavina<sup>3</sup>,  
Marina Mikhailovna Krekova<sup>4</sup> and Alexander Markov<sup>5</sup>**

<sup>1</sup>*Pavlov First Saint Petersburg State Medical University, L'va Tolstogo Str. 6-8, Saint Petersburg, 197022, Russia.*

<sup>2</sup>*North-Western State Medical University (Named after I.I. Mechnikov), St. Petersburg, Street Kirochnaya 41, 191015, Russia.*

<sup>3</sup>*Saratov State Medical University (Named after V. I. Razumovsky), Street Bolshaya Kazachya 112, 410012, Russia.*

<sup>4</sup>*Moscow Polytechnic University, Russia.*

<sup>5</sup>*Tyumen State Medical University / Tyumen Industrial University, Tyumen, Russian Federation.*

### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i48A33236

*Editor(s):*

(1) Dr. Giuseppe Murdaca, University of Genoa, Italy.

*Reviewers:*

(1) Dhruvo Jyoti Sen, Techno India University, India.

(2) Tapan K. Chaudhuri, Eastern Virginia Medical School, USA.

(3) R. S. Chandan, JSS Academy of Higher Education & Research, India.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/76209>

**Short Research Article**

**Received 28 August 2021**

**Accepted 01 November 2021**

**Published 06 November 2021**

### **ABSTRACT**

The article examines allergic reactions of the body to drugs used in dental practice. The authors note that adverse or allergic reactions of medicines to the human body are possible with any medications that are prescribed or administered in a dental office. Although most of the pharmacological agents used today have a favorable profile and they are relatively safe, a modern specialist should be aware of potential adverse reactions that may occur and one should be ready to cope with any complications.

Adverse or allergic reactions are possible when working with drugs such as local anesthetics, sedatives, analgesics and antibiotics, for this reason, it is necessary to study the possible reactions

of the patient's body to them when administering such drugs to reduce the negative impact on the body. In general, the pharmacological arsenal of a practicing dentist is relatively safe today. However, a prudent clinician should be aware of potential adverse reactions that may occur as a result of taking medications, and be confident in the treatment of such complications.

*Keywords: Allergic reaction; drugs; dental practice.*

## 1. INTRODUCTION

An adverse drug reaction (ADR) can be defined as any undesirable effect of a drug. It is important to distinguish between ADR and allergy: allergy refers to an immuno-mediated reaction to a drug, such as anaphylaxis, whereas ADR can be any effect that is not therapeutically desirable, such as sedation. In fact, an allergy can be an example of ADR, but not all ADRs are an allergy [1].

True drug allergy can be determined by a specific immunological mechanism (T-lymphocytes or drug antibodies). Such reactions occur immediately or after a delay and can be life-threatening for the patient. Direct drug allergy usually manifests itself in the form of urticaria, rhinitis, angioedema, bronchospasm, conjunctivitis, gastrointestinal disorder or anaphylaxis (which can cause cardiovascular collapse) [2].

Delayed drug allergy usually manifests on the skin with possible symptoms, including delayed urticaria, spotty papular rashes, vasculitis and blistering diseases. If a practitioner is concerned about an allergic reaction to a drug in a patient, he should immediately stop taking the suspected drug, treat the reaction, document the medications taken (dose, type, duration) and record any signs and symptoms. In severe cases, an ambulance should be called and the patient should be accompanied to the nearest emergency department. The patient should be referred to a family doctor for further allergy examination.

## 2. MATERIALS AND METHODS

When writing the article, comparative method was used, as well as an array of information was studied within the framework of the research topic.

## 3. RESULTS

Pharmacotherapy has been described as a serious cause of both mortality and is directly

related to the occurrence of adverse events. Patients in the intensive care unit are more vulnerable to the occurrence of ADR [3]. The characteristics inherent in the complexity of their clinical condition, monitoring devices, invasive procedures and the wider use of drugs, especially those with narrow therapeutic indices or those administered parenterally, make them more susceptible to damage as a result of pharmacological therapy.

Pharmacovigilance enhances the safety of drugs after they enter the market by evaluating, detecting, preventing and understanding the side effects of drugs or any other drug-related problems. Reporting of adverse drug reactions (ADR) is the basis of pharmacovigilance and identifies undesirable effects of a drug that occur with normal clinical use. Adverse reactions are common causes of mortality and morbidity worldwide and represent a fundamental economic burden for any given healthcare system.

Adverse reactions occurring in medical practice cannot always be predicted based on pre-market data due to internal limitations of clinical trials, such as insufficient number of patients and limited follow-up time. Therefore, post-marketing surveillance is a necessary tool for early detection of severe and unexpected adverse reactions.

ADRs cause two million hospitalizations and one million emergency department visits annually.

A significant and massive increase in drug consumption leads to an increase in the number of ADRs. ADR can be defined as unintentional injuries that may occur at any therapeutic concentration and may be harmful and require hospitalization. At the same time, there are both ADR and non-negative reactions of the body in case of an error in taking medications (ETM). ETM is either a decrease in effectiveness or an increase in the risk of harm during treatment (i.e., an error in the treatment process that can harm the patient) [4].

ADRs are common and can cause significant morbidity and mortality. A study conducted in the UK showed that 12% of primary care patients are exposed to ADR due to errors in prescribing. This percentage increased to 38% among the elderly and 30% among patients with polypragmasia taking five or more medications.

In modern dental practice, only a few categories of pharmacological agents are widely used; these include local anesthetics (LA), central nervous system depressants (for example, nitrous oxide, benzodiazepines and general anesthetics), analgesics (for example, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen and opioids) and antibiotics (for example, penicillin, clindamycin and metronidazole) [5].

It is extremely important that the dental medical team is well equipped to manage any predictable and unforeseen adverse reactions that occur in the dental office. In addition, a healthcare professional is responsible for carefully understanding the health status of their patients when prescribing new medications or changing dosages, so as not to provoke unwanted adverse reactions that could have been avoided.

Local anesthetics (LA) are the most commonly used drugs in dental practice. LA are generally considered safe; however, the practitioner should take responsibility for ensuring that the dosage and concentration are adapted for each patient to avoid potential adverse reactions, both local and systemic [6].

Local complications associated with the administration of LA include tissue necrosis and direct neurotoxicity. Tissue necrosis occurs due to the destruction of the tissue supplying the vessels, and is associated with the irritating nature of the solution injected in large volumes or narrowing of the vascular network using vasoconstrictors in the cartridge of LA (for example, adrenaline or levonordephrine). Treatment of these conditions is mostly symptomatic and should be avoided. Careful administration of LA, especially in the area of tightly bound tissues such as the palate, will reduce the likelihood of ischemia.

It has been reported in the literature that direct neurotoxicity with respect to nerve trunks, leading to paresthesia, is more common with anesthetic solutions of higher concentration, such as 4% articaine and prilocaine, when

administered in the form of blocks. Other authors have suggested that this may not be the case when using articaine. The doctor should carefully weigh whether the benefits of a 4% solution outweigh the likelihood of complications. Treatment of paresthesia includes observation and possible referral to a dental surgeon with experience and knowledge in the treatment of these conditions. Fortunately, in most cases, paresthesia is temporary and lasts for 8 weeks; however, in some cases, neurological deficits may be permanent. Other complications associated with LA are a combination of ADR and a technique such as intramuscular injection leading to the locked jaw [7].

Since LA affects the cardiovascular system, systemic complications may occur. All LA are depressants of the central nervous system and can cause drowsiness, convulsions and even coma at sufficiently high blood levels in the cerebral circulation. Although this is unlikely in adult patients, except for excessive administration of LA, it is much more dangerous for pediatric patients with much lower body weight. Clinicians should be aware of the calculations of the maximum dosages of LA.

Another possible systemic ADR may be methemoglobinemia, an unusual reaction most often associated with prilocaine and local benzocaine. Methemoglobinemia leads to cyanosis, which does not respond to 100% oxygen, and can cause nausea, sedation, seizures and coma at high levels. Patients with congenital methemoglobinemia should avoid the use of these anesthetics [8].

Today, the most common vasoconstrictor in LA formulations is adrenaline, which is available in formulations of 1:50,000, 1:100,000 and 1:200,000. Adrenaline is a potent cardiovascular agent, and in high doses can lead to increased heart rate, blood pressure and the potential danger of cardiovascular diseases. The clinician should be careful about the amount of the drug administered.

#### 4. DISCUSSION

All sedatives and general anesthetics can cause respiratory depression depending on the dose, and the intensity of depression increases faster with the introduction of several sedatives. It is important to distinguish physiological respiratory depression from anatomical, i.e. caused by loss of muscle tone. The loss of muscle tone of the

pharyngeal musculature, as well as the incorrect position of the tongue, reduces the patency of the pharynx. Such anatomical obstruction can occur at any level of sedative effect and can be eliminated using methods of airway passage, such as head tilt, chin lift or oropharyngeal airways [9].

Psychological depression is associated with changes in the mechanisms associated with breathing. Respiration depends on both the central hypercapnic drive and the peripheral hypoxic drive, and the classes of sedatives affect these drives in different ways. As the doses increase, the differences become more and more minimal, and this affects both the central and peripheral drives. As for respiratory volume and respiratory rate, in general, inhaled anesthetics (for example, sevoflurane) reduce respiratory volume by increasing respiratory rate, while intravenous agents and opioids suppress both. Benzodiazepines depress breathing to the least degree. In addition to respiratory effects, sedatives and general anesthetics also affect the cardiovascular system and can lead to changes in heart rate and blood pressure.

It is also worth considering the continuum of sedative effect. With minimal sedation ("anxiolysis"), patients respond normally to verbal stimulation. With moderate sedation ("conscious sedation"), there is a purposeful reaction to verbal or tactile stimulation. Deep sedation involves a purposeful response to a repetitive or painful stimulus. With general anesthesia, the patient does not respond to pain. A purposeful reaction should not be considered as a rejection of a painful stimulus.

Acetaminophen is one of the safest analgesics available, causing virtually no side effects when administered to healthy people in normal doses.

The most significant side effect associated with acetaminophen is hepatotoxicity. Hepatotoxicity occurs due to the accumulation of N-acetyl-para-benzoquinone imine (NAPQI), a potentially toxic metabolite of acetaminophen. This metabolite is formed from about 5% -15% of the total intake of acetaminophen, and the remaining 85% -95% are immediately excreted by the kidneys after sulfation or glucuronidation. In healthy people, NAPQI is conjugated with glutathione and is also excreted from the body. However, in the presence of excessive doses of paracetamol or in people with impaired hepato function, hepatotoxicity becomes a serious problem.

The generally accepted maximum dose of paracetamol for a healthy person is 4 grams per day; however, recently it has been proposed to reduce this dose to 3 grams per day. Hepatotoxicity may occur when a large bolus is administered at a dose of 7.5-10 g for adults (150 mg / kg for children) with a potentially fatal outcome at a dose of 20-25 g. Since the dosage causing hepatotoxicity is approximately twice the daily maximum dose, the probability of adverse reactions is low, provided that proper instructions for the drug are given. In case of overdose, patients should be prescribed high doses of acetylcysteine to restore the stores of the enzyme glutathione.

You should also pay attention to nonsteroidal anti-inflammatory drugs. Although they are usually well tolerated, the most frequent adverse reactions associated with NSAIDs are associated with gastrointestinal complications, and the most dangerous are gastrointestinal bleeding and toxicity. Gastrointestinal toxicity is not considered uncommon: more than 16,500 deaths worldwide have been attributed to NSAIDs. Gastrointestinal bleeding occurs due to the mechanism of action of NSAIDs, which inhibit the synthesis of prostaglandins, thereby reducing the protective effect of prostaglandins on the mucous membrane. Therefore, a prudent doctor should avoid prescribing NSAIDs to any patient with a history of gastric ulcer or bleeding and should consider paracetamol as an alternative drug [10].

Less often there is an opportunity to provoke an anaphylactoid reaction with NSAIDs. Bronchospasm and other signs and symptoms of allergy may occur in susceptible patients due to the leukotriene pathway of action. In patients suffering from severe asthma, the doctor should avoid taking NSAIDs, as well as acetylsalicylic acid. Other possible adverse reactions include impaired renal function; however, they usually require long-term chronic administration of NSAIDs.

It is also necessary to stop at the consideration of opioids. All opioids cause dose-dependent respiratory depression, sedation and gastrointestinal upset, including constipation, nausea and vomiting. Mood changes are also possible, which may manifest as euphoria or dysphoria. Unfortunately, opioid abuse and addiction are growing at an appalling rate across Canada and the US, to the point that it is now considered an "opioid crisis."

Patients suffering from opioid use disorder often require long-term treatment, most often with methadone, to maintain recovery. Dentists who prescribe approximately 12% of all opioids in North America should try to avoid prescriptions for opioids, except in cases of extreme necessity for the recommended protocol of postoperative anesthesia. Prescriptions for opioids should be written out wisely after a thorough study of the patient's medical history in order to minimize the risk of the patient developing physical dependence, a destructive side effect of opioid drugs.

If we talk about the use of antibiotics, then, with the exception of anaphylactic reactions, the most commonly used antibiotics in dentistry today are well tolerated. The most common adverse reaction for all antibiotics is associated with a gastrointestinal disorder (for example, diarrhea, nausea, vomiting). Approximately 2-10% of all antibiotics used cause diarrhea, reaching 25% in the case of Augmentin (amoxicillin and clavulanic acid).

The possibility of developing more serious opportunistic infections, such as *Clostridium difficile* or yeast infections, after taking antibiotics is of more concern. The first is most often associated with the use of clindamycin, although any antibiotic can potentially cause *C. difficile* infection. If the patient suspects that he may have a *C. difficile* infection, he should immediately contact his family doctor for an examination. In cases where the patient does not have a family doctor or has serious symptoms, such as bloody diarrhea or urine, he should contact the nearest hospital in the emergency department. Fungal infections are usually treated by prescribing a topical antifungal agent such as nystatin.

It is also extremely important to inform patients about their limitations when taking certain antibiotics in order to avoid potential adverse reactions. Users who are prescribed metronidazole, an antibiotic effective in the treatment of anaerobic bacterial infections, should be advised to avoid alcohol consumption due to the ability of metronidazole to inhibit enzymes in the ethanol decomposition pathway. Patients may experience hot flashes, headaches, nausea, and palpitations. Metronidazole users should avoid drinking alcohol for at least 3 days after completing a full course of antibiotics [11].

Another, more life-threatening side effect of drugs is the interaction of clarithromycin,

erythromycin and azithromycin with digoxin. These antibiotics inhibit the excretion of digoxin from the bloodstream and thus have the potential to seriously raise the level of digoxin in the blood, which leads to intoxication. Signs of digitalis toxicity usually include nausea, vomiting, and an irregular heartbeat. Less common symptoms may include confusion, blurred vision, and swelling of the extremities.

## 5. CONCLUSION

In general, the pharmacological arsenal of a practicing dentist is relatively safe today. However, a prudent clinician should be aware of potential adverse reactions that may occur as a result of taking medications, and be confident in the treatment of such complications.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Edwards IR, Aronson JK Adverse drug reactions: definitions, diagnosis, and management *Lancet*. 2000;356(9237):1255-1259.
2. Pourpak Z, Fazlollahi MR, Fattahi F Understanding adverse drug reactions and drug allergies: principles, diagnosis and treatment aspects *Recent Pat Inflamm Allergy Drug Discov*. 2008;2(1):24-46
3. Limsuwan T, Demoly P Acute symptoms of drug hypersensitivity (urticaria, angioedema, anaphylaxis, anaphylactic shock) *Med Clin North Am*, 2010;94:691-710.
4. Demoly P, Adkinson NF, Brockow K, *et al*. International Consensus on drug allergy *Allergy*, 2014;69 (4):420-437.
5. Garisto GA, Gaffen AS, Lawrence HP, *et al*. Occurrence of paresthesia after dental local anesthetic administration in the United States *J Am Dent Assoc*, 2010;141 (7):836-844.
6. DiRenzo KV, Lim JL, Albalawi F, *et al*. Differential effects of sodium channel

- blockers on neural survival and responsiveness: 2% lidocaine kills more SHSY-5Y cells and reduces cellular activity as compared to 4% articaine J Den Res, 2016;95:0790.
7. Volkow ND, Collins FS The role of science in addressing the opioid crisis N Eng J Med, 2017;377 (4):391-394.
  8. Dione R Breaking down barriers to care with effective pain management Compendium., 2016;37(5):346-348.
  9. E. Montané, J. Santesmases Adverse drug reactions Med. Clin. (Barc);2020.
  10. M.M. Fry, C. Dacey Factors contributing to incidents in medicine administration. Part 2Br. J. Nurs., 2007;16:676-681.
  11. T. Dilles, M.M. Elseviers, B. Van Rompaey, L.M. Van Bortel, R.R.V. Stichele Barriers for Nurses to Safe Medication Management in Nursing Homes J. Nurs. Scholarsh., 2011;43:171-180.

---

© 2021 Shefova et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*

*The peer review history for this paper can be accessed here:*  
<https://www.sdiarticle4.com/review-history/76209>