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DPT (DOSE PROVOCATIVE TEST) TEST FOR PROVING ALLERGIC REACTIONS TO LOCAL ANAESTHETICS

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Abstract: To prove the existence of possible allergic reaction to local anaesthetic by the recommendations and experience of the current literature, an assortment or mosaic of complementary diagnostic tests is made by: anamnesis and a clinical picture and *in vivo* skin allergy tests – tests of the humeral and cellular immune response. Anamnesis and the clinical picture are mostly in metaphorical characteristics because we are not direct observers of the happenings and manifestations.

If we use anaesthetics every day there is a possibility of side effects. The main aim is to determine the real persistance of hypersensitive reactions.

For diagnosing the hypersensitive reactions in this task, *in vivo* tests were done on 50 examinees with plus (+) anamnesis for unwanted reactions from previous anesthetics applications (tooth extraction). The accent is put on the DPT (dose provocation test).

Based on SAT allergic testing the percentage is 4.0%.

We used the relative statement of the patient as support for the real picture of the event. The DPT test is considered the only *in vivo* test that may exclude the risk of allergic reaction, because of its specificity and high risk. Besides the negative resultes from DPT we cannot be absolutely sure and rely on the test results, including the results of anaesthetic application, because the risk of allergic reaction of patients who have been tested is not higher than that of the patients who have not been tested.

Key words: KAT-allergy skin test, sc DPT subcutaneous dose incremental re challenge test, allergic reaction.

Introduction

The drug allergic/hypersensitive reaction presents an indirect immune answer to the pharmacological agents and pharmacological receiver. Anaphylaxis is the toughest form of allergic reaction, and it comes as the result of antigen – IgE antibody reaction. The first exposition of the antigen or a substance with a similar structure was before the reaction. The organism made IgE antibodies to the agent and sensitivity resulted.

Permanent intake into the organism of drugs with a large molecular weight is in most of cases linked to an immune and anaphilactic reaction. In the meanwhile, plenty of the drugs with a light molecular weight which are taken cause contact dermatitis.

The local anaesthetics and their products are united in their light molecular weight and they cannot cause an allergic reaction. Because they belong to the hapten group, at the time of their biotransformation they usually bind covalently with macromolecule (tissue protein) as a carrier causing an immune antigen antibody reaction (Escolano F., Alago L. [3]). Gell and Coombs classify early sensibility into types 1, 2 and 3; type 4 belongs to late sensibilisation (Keri *et al.* [7]).

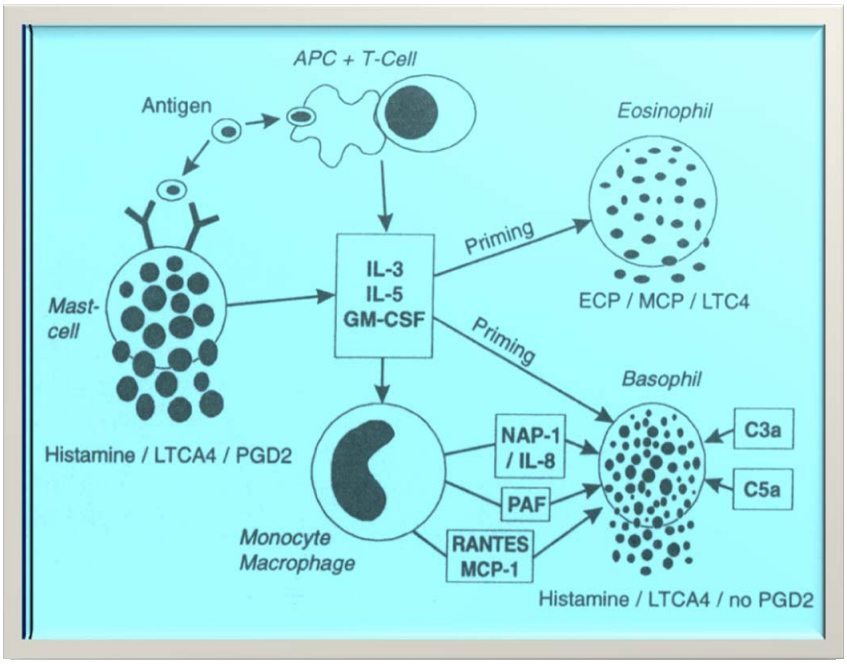


Figure1 – Types of allergic reaction
Слика 1 – Типови на алергиска реакција

Type 1 – The reaction appears within seconds up to a few hours and it is in correlation with the allergens invasion.

Type 2 – The reaction is a result of IgEe and IgM interaction with the complement, causing citotoxic reactions.

Type 3 – Reaction of immune response which results in infiltration into vascular or connective tissue.

Type 4 – The reaction is in mediation of sensitive Ly which appears mostly after 48 hours from the exposure.

Allergic reactions are not rare appearance in dental practice, but the true reactions appear rarely. The reactions of hypersensitivity to local anaesthetics are mainly limited to ester type anaesthetics. But there is another type of anaesthetic (the amide group) which contains paraben, metilparaben or p-hydro xybenzoat and they also can cause an allergic reaction. Keri *et al*. [7]

According to Petrovic [12] the allergic reactions caused by ester type anaesthetics are 6% more common than those from the amide type anesthetics. The cross reaction between both types are not recorded, although ester type cross reactions were recorded. Amide type cross reactions were not evidenced or recorded. When antibodies are not included in the reaction,that reaction is called an anaphylactoid reaction. Clinically it is not easy to differentiate between anaphylactic and anaphylactoid reactions. Reactions which are dangerous to life often happen in individuals with a positive anamnesis of allergy, atopic or asthma. Although these patients often prepare with corticosteroids, there is no data that real anaphylaxes would eventually be stopped.

Verification of suspect allergic reactions to local anaesthetics is a complex diagnostic process. For safer use of local anaesthetic we need to use SAT (Skin Allergy Test) (Naguib *et al*. [10]. Imagined as a simulation of the event, the skin test should provoke the allergic reaction in a controlled/easy form. The only defect is the rare but possible risk of anaphylaxis if we use undiluted solutions, so that is why we should have anti-shock therapy (Balabanova-Stefanova M., Ezova N. *et al*., Le Sellin *et al*. [1, 5, 8]).

Preventive measures are: taking good anamnesis for similar symptoms of at the time of extraction of teeth or giving anaesthesia, sickness, weakness, asphyxia, allergic reaction and other drugs, family anamnesis and any other therapies or allergic tests.

The possibility of the appearance of unwanted reactions after the daily based application of anaesthetics is more often and that is why this testing is done.

- Defining the real representation of the hypersensitive reaction to local anesthetics, based on allergic testing.

- Defining the possibility of cross reaction between anaesthetics of the same type.
- Defining a group of patients who will undergo allergic examination

Materials and methods

This work presents a retrospective study which includes 50 examinees with (+) anamnesis for unwanted reactions to previous anaesthetics application (tooth extraction). Both genders are included and the age of the patients is from 7–77.

In the control group are all the patients who, following verification or negation of an allergic reaction, did not indicate an absolute assurance for excluding the allergic reaction. All the data from the examinees are put into a questionnaire from which we know enough information about the agent and reaction, specifics about the patient and the need for further testing.

For diagnosing the hypersensitive reactions in this work *in vivo* tests were used and the accent put on the DPT (dose provocation test). The DPT was made after we had negative results from the SAT, Prick and ID tests. The testing was done according to the instructions of Vervloet and Pradal [13].

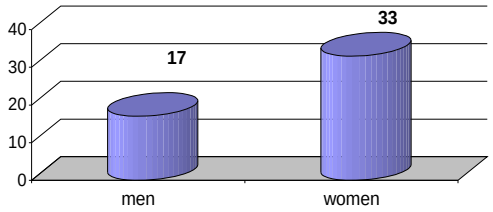
The protocol for performing the test is the following: the test is performed on the lower arm in several steps. The dose and the concentration are gradually increased. It begins with diluted solutions whose dilution follows a defined order: 1 : 10000, 1 : 1000, 1 : 100. 1 : 10 and 1 : 1 at time intervals of 15 minutes. Finally the undiluted anaesthetic which will be used for the intervention is given in the same dose and concentration.

SAT and DPT are done with anaesthetics from the amide group, which do not contain adrenalin and are determined by the dentist. In this case Lidocaine and Mepivacaine were used.

Results

Of the total of examinees who were tested with SAT and DPT, 33 were women, 17 were men. The ratio 1 : 2 in favour of women shows that women are more exposed to allergic reaction. That relation can be seen in Graph 1.

Graph 1. Examinees with positive anamnesis of allergic reaction with DPT testing: distributed by gender.



Graph 1 – Distribution by gender
Графикон 1 – Дистрибуција по пол

In the percentage representation of age groups the most common is the group with an age limit from 28–37 years, with 24%, and the group from 38–47 years with 20%. This is shown in Table 1.

Table 1. Examinees with positive anamnesis to allergic reactions tested with DPT: distributed by age

Table 1 – Табела 1

Distribution by gender
Дистрибуција според возрасти

Age	Absolute number	Relative number %
7–17	6	12
18–27	8	16
28–37	12	24
38–47	10	20
48–57	8	16
58–67	3	6
68–77	2	4
> 78	1	2

Possibly this is the period in which most patients call at the dentist and are in contact with local anaesthetics application (extraction of teeth most common).

After the SAT test, DPT tests were made on the examinees who were negative, with two kinds of anaesthetics of the amide type group: Lidocaine in 60% of the cases and Mepivacaine in 40%. In both cases the results were negative. We should say that this kind of testing was done only on patients with negative skin allergy tests.

After the tests, an appropriate anaesthetic was used on these patients and no unwanted complications were recorded, although they were in different directions. The results of DPT are given in Table 2 and Graph 2.

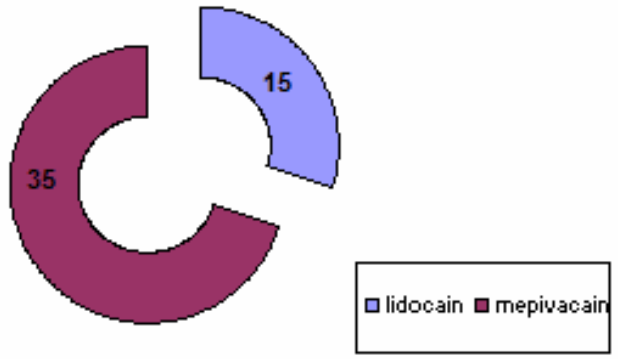
Table 2 – Табела 2

Distribution according to results obtained from skin tests
Дистрибуција според резултатите добиени од позитивните тестирања

Tested	*SAT*				Sc DPT				Total
Anaesthetics	Absolute number		Relative number		Absolute number		Relative number		
	"+" test	"-" test	"+" test	"-" test	"+" test	"-" test	"+" test	"-" test	
Lidocaine	2	13	4%	36%	/	13	/	36%	15 40%
Mepivacaine	/	35	/	60%	/	35	/	60%	35 60%

Table 2 Examinees with positive anamnesis for allergic reactions who were tested with SAT and DPT: distributed by results obtained from skin testing.

Graph 2 Examinees with positive anamnesis for allergic reactions who were tested with sc DPT: distributed according to the tested anaesthetic.



Graph 2 – Distribution according to anaesthetics tested
Графикон 2 – Дистрибуција според тестираниот анестетик

Table 3 – Табела 3

Distribution according to anaesthetics tested
Дистрибуција според тестираниот анестетик

Anaesthetic	Relative number %	Absolute number
Lidocaine	40%	15
Mepivacaine	60%	35

Table 3 Examinees with positive anamnesis for allergic reactions who were tested with sc DPT: distribution according to the tested anaesthetic.

Discussion

It is thought that the problem of the allergy is a little confused, unsolved and not sufficiently treated, because of the nature of the illness. SAT tests have been used for a century and they still endure today (Solter, Blackey, Jadason). With SAT tests as the most simple, fast and also in the phase of testing there may be found clinic manifestations of sensibility to the tested allergen in patients with a latent or manifest atopic predisposition.

From *in vivo* tests, sc DPT is the most frequently commented on of the other SATs, because of its high risk and gold standard quality and as key evidence of allergic reaction to anaesthetics.

Because of its specific high risk, the test counts as the most reliable for confirmation or rejection of the possibility of allergic reaction. For realization of the cause this test is done on patients from the category with a high risk of anaphylaxis. Before approaching the DPT test on the patient SAT tests must be done, which must be negative.

Although allergic reactions are considered as rare, they do appear in dental interventions. According to Sandra R. Knowles [11] and others, the percentage is 2.5–10%, of all unwanted reactions (Ezova N., Milgrom P., Fiset L. [5, 9]. The positive (+) results from the tests is 4%, and is in correlation with the results from other authors, e.g. Le Sellin [8], Vervolet and Pradal [13]. Our results are in correlation with the results by D'Athis [2] in that the anaesthetics can produce an allergic reaction. Our tests comfirm that anaesthetics do not cross between themselves , like the comfirmation by Keri [7]. Hain, Ezova, Le Sellin [6, 5, 8] and other authors refer to cases with positive results from SAT testings done with local anaesthetics to groups of patients with positive anamnesis for unwanted reactions.

Patients with a positive personal and family anamnesis are more exposed to allergy because of their genetic predisposition to creating IgE. Atopic patients do not have a larger risk of creating IgE Anaphylaxis than non-atopic patients. It is calculated that every cell membrane has 40 000–100 000 receptors potentially open to interact with IgE (Robert K., Stoelting M.D [4]).

The most important risk elements for hypersensitivity to drugs are chemistry characteristics, molecular weight, the dose, method of administration, time of treatment, reapplication of drugs and various illnesses.

From the analysis of the results we may say that:

1. Although very rare, allergic reactions to local anaesthetics do exist. Based on the SAT allergic test the percentage is 4.0%.
2. Based on SAT and DPT, there is no cross-reaction between Mepivacaine and Lidocaine.
3. In cases where anamnesis shows anaphylaxis, skin tests are needed.
4. The time interval between the SAT and application of the ana esthe tics needs to be short, because the possibility of sensibility is not excluded.
5. DPT remains the "gold standard" among the tests , we recommend it after getting a negative reaction from the previous tests and when we need to exclude anaesthetic reaction.
6. After the test, based on the results we can use the drug which is tested with DPT with confidence.

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DPT (ДОЗНО ПРОВОКАТИВЕН ТЕСТ) ТЕСТ ЗА ДОКАЖУВАЊЕ НА АЛЕРГИСКИ РЕАКЦИИ НА ЛОКАЛНИ АНЕСТЕТИЦИ

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За докажување од постоење на можна алергиска реакција на локални анестетици според препораките и искуствата на актуелната литература, асортиманот или мозаикот на комплементарни дијагностички тестови го чинат: покрај анамнезата и клиничката слика и "in vivo" кожните алерголошки тестови – тестови на хуморален и целуларен имунолошки одговор. Анамнезата и клиничката слика се најчесто во преносно својство, бидејќи ние не сме директни опсерватори во збиднувањата што се случиле и како се изманифестирале, туку се потпираме на релативни искази од пациентот за вистинската слика на настанот.

Секојдневната употреба на локалните анестетици може да даде несакани ефекти. Главната цел е да се докаже вистинско присуство на хиперсензитивна реакција.

За дијагностицирање на хиперсензитивните реакции во овој труд се користени "in vivo" алерголошки тестирања, кај 50 испитаници со (+) позитивен анамнестички податок за некоја несакана реакција при претходно давање на анестезија (вадење на заб). Посебен акцент е даден на сц DPT (субкутан дозно провокативен тест).

Врз основа на нашите КАТ алерголошки тестирања на локални анестетици, процентуалната застапеност на истите изнесува 4,0%.

За дозно провокативниот тест се смета дека е единствениот "in vivo" тест што може да го исклучи ризикот од алергиска реакција, поради својата специфичност и висока ризичност.

И покрај негативно добиените резултати од тестот не можеме никогаш да бидеме апсолутно сигурни и да се потпреме на резултатите од тестот, како и во исходот на апликација на анестетикот, бидејќи ризикот од последователна алергиска реакција, кај тестирани лица не е поголем отколку кај оние пациенти на кои не им се извршени соодветни тестирања.

Клучни зборови: КАТ – кожни алерголошки тестирања, сц. ДПТ (субкутан дозно провокативен тест), алергиски реакции.

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