PREVALENCE OF SENSITIZATION TO DRUGS IN ANESTHESIOLOGY

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ABSTRACT.

Introduction. Both underdiagnosis and overdiagnosis of sensitization to drugs are problems in the contemporary allergology practice.

The aim of the present study is to investigate the sensitization to drugs, used in anesthesiology practice in patients with medical records, demonstrating sensitization to anesthesiology drugs were included.

Patients and Methods. In the present prospective study 356 patients [men – 109(30.62%); mean age 51,98 years (SD 20.19), women – 277(69,38%); mean age54,49 (SD 18.97) tested in the Allergology Union of the Inner Consulting Department, UMHAT "Sv. Georgi" - Plovdiv (August 2014 – January 2015), with medical records demonstrating sensitization to anesthesiology drugs. A detailed clinical history was taken and dermal prick-tests with anesthesiology drugs were performed as recommended by International consensus on drug allergy of European Academy of Allergy and Clinical immunology (EAACI).

Results. Sensitisation was established in 107 (30,06%) of patients. Monosenzitised were 42 (39,25%) and 65 (60,75%) were polysenzitised. The following sensitizations were established: Thiopental – 2; Fentanyl – 10; Chyrocain – 7; Atropine sulfate – 15; Ketamine – 14; Suxamethonium – 12; Pancuronium - 2; Pipecuronium – 12; Diazepam – 4; Galantamine – 59; Lidocaine – 7; Bupivacain – 5; Propofol – 5; Midazolam – 2; Pethidine – 59.

Conclusion. The study established overdiagnosis in assessment of sensitization to drugs, used in anesthesiology practice. The overcome of overdiagnosis requires following the recommendations of International consensus on drug allergy. Prick test with drugs with standard concentrations as recommended by ENDA/ EAACI, carried out by highly skilled stuff can guarantee the proper diagnosis work up.

Keywords: *sensitization, anesthetics, prick-test.*

Introduction.

Allergic reactions that occur under anesthesia are significant causes of perioperative morbidity and mortality (5). They can be life-threatening, may require or prolong hospitalization, and may necessitate changes in subsequent therapy. Both underdiagnosis (due to under-reporting) and overdiagnosis are common. A definitive diagnosis of such reactions is required in order to institute adequate treatment options and proper preventive measures. The use of standardized systematic approaches for the diagnosis can improve outcomes (4).

In order to predict which patients might experience allergic reactions, it is essential to determine the risk factors. Patients at risk of perioperative allergy are those who are allergic, as established by performing proper allergological tests, to any of the drugs to be administered during anesthesia, as well as those who have had a reaction during a pervious general anesthesia that remains unexplained (6).

The patient's history is crucial to suspect a drug allergy. But to base the diagnosis on history alone is an unreliable indicator of true hypersensitivity. Skin tests are essential for the diagnosis.

A standardized procedure how to do skin tests containing general considerations has been published by European Network on Drug Allergy (ENDA)/(8). To promote and standardize reproducible skin testing with safe and nonirritant drug concentrations in the clinical practice, ENDA and European Academy of Allergy and Clinical Immunology (EAACI) Interest Group on Drug Allergy has published a position paper on skin test concentrations (1). Consequently, the

International Collaboration in Asthma, Allergy and Immunology (iCAALL), formed by EAACI, the American Academy of Allergy, Asthma and Immunology (AAAAI), the American College of Allergy, Asthma and Immunology (ACAAI), and the World Allergy Organization (WAO), has decided to issue an International CONsensus (ICON) on drug allergy. The purpose is to provide a comprehensive reference document for the diagnosis and management of drug hypersensitivity reactions (2,3).

Skin prick test (SPT) is considered to be the standardized dermal test, performed with standard concentrations for administered drugs. Scratch tests are not recommended in the consensus because they are poorly standardized.

The aim of the present study is to investigate the sensitization to drugs, used in anesthesiology practice in patients with medical records, demonstrating sensitization to anesthesiology drugs were included.

Patients and Methods. In the present prospective study 356 patients [men – 109(30.62%); mean age 51,98 years (SD 20.19), women – 277(69,38%); mean age54,49 (SD 18.97) tested in the Allergology Union of the Inner Consulting Department, UMHAT "Sv. Georgi" - Plovdiv (August 2014 – January 2015), with medical records, demonstrating sensitization to anesthesiology drugs were included. A detailed clinical history was taken and dermal prick-tests with anesthesiology drugs were performed as recommended by International consensus on drug allergy of European Academy of Allergy and Clinical immunology (EAACI). SPT was done on the volar surface of the forearm. A drop of the drug was placed on the skin with the distance between tests at least 2 cm to avoid cross-contamination. The skin was pricked through the drop with 1 mm prick lancets. Histamine hydrochloride 10mg/ml and physiological saline were used as positive and negative controls respectively. A skin prick test was considered positive when the wheal diameter was 3 mm larger than that produced by the negative control after 15 minutes. The tests were performed with the concentrations, recommended by ENDA/EAACI position paper (tabl. 1)

Concentration of drugs, used in the anesthesiology practice **Table 1.**

Drug		SPT	
Generic name	Undiluted concentration(mg/ml)	Dilution	Maximum concentration mg/ml)
Thiopental	25	Undiluted	25
Fentanyl	0.05	Undiluted	0.05
Chyrocaine	2.5	Undiluted	2.5
Atropine sulfate	1	Undiluted	1
Ketamine	10	Undiluted	10
Suxamethonium	50	1/5	10
Pancuronium	2	Undiluted	2
Pipecuronium	2	Undiluted	2
Diazepam	5	Undiluted	5
Galantamine	1	Undiluted	1
Lidocaine	5	Undiluted	5
Bupivacain	5	Undiluted	5
Propofol	10	Undiluted	10
Midazolam	5	Undiluted	5
Pethidine	50	Undiluted	50
Atracutium	10	1/10	1

Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics 20 software (Chicago, IL, USA). Fisher's exact test was used for the comparison of number of patients, reported sensitization and patients with established sensitization (*P*-value < 0.05 was regarded as statistically significant).

Results.

Out of 356 patients with documented sensitization to drugs, used in anesthesiology practice, sensitization was established in 107 (30,06%) only. The following sensitizations were established: Thiopental – 2 (0.93%); Fentanyl – 10 (4.65%); Chyrocain – 7 (3.26%); Atropine sulfate – 15 (6.98%); Ketamine – 14 (6.51%); Suxamethonium – 12 (5.58%); Pancuronium – 2 (0.93%); Pipecuronium – 12 (5.58%); Diazepam – 4 (1.86%); Galantamine – 59 (27.44%); Lidocaine – 7 (3.26%); Bupivacain – 5 (2.33%); Propofol – 5 (2.33%); Midazolam – 2 (0.93%); Pethidine – 59 (27.44%). Monosenzitised were 42 (39.25%) of patients and 65 (60.75%) were polysenzitised (tabl. 2, fig. 1).

Sensitization to drugs, used in anesthesiology practice **Table 2.**

Drug	Sensitization		
	Reported	Established	P
Thiopental	18	2	< 0,001
Fentanyl	35	10	< 0,001
Hyrocain	20	7	< 0,001
Artopin	62	15	< 0,001
Ketalar	25	14	< 0,001
Suxamethonium	52	12	< 0,001
Pancuronium	10	2	< 0,001
Pipecuronium	21	12	< 0,025
Diazepam	26	4	< 0,001
Nivalin	99	59	< 0,001
Lidocain	33	7	< 0,001
Maracain	21	5	< 0,001
Propofol	19	5	< 0,001
Dormicum	10	2	< 0,001
Pethidine	91	59	< 0,001

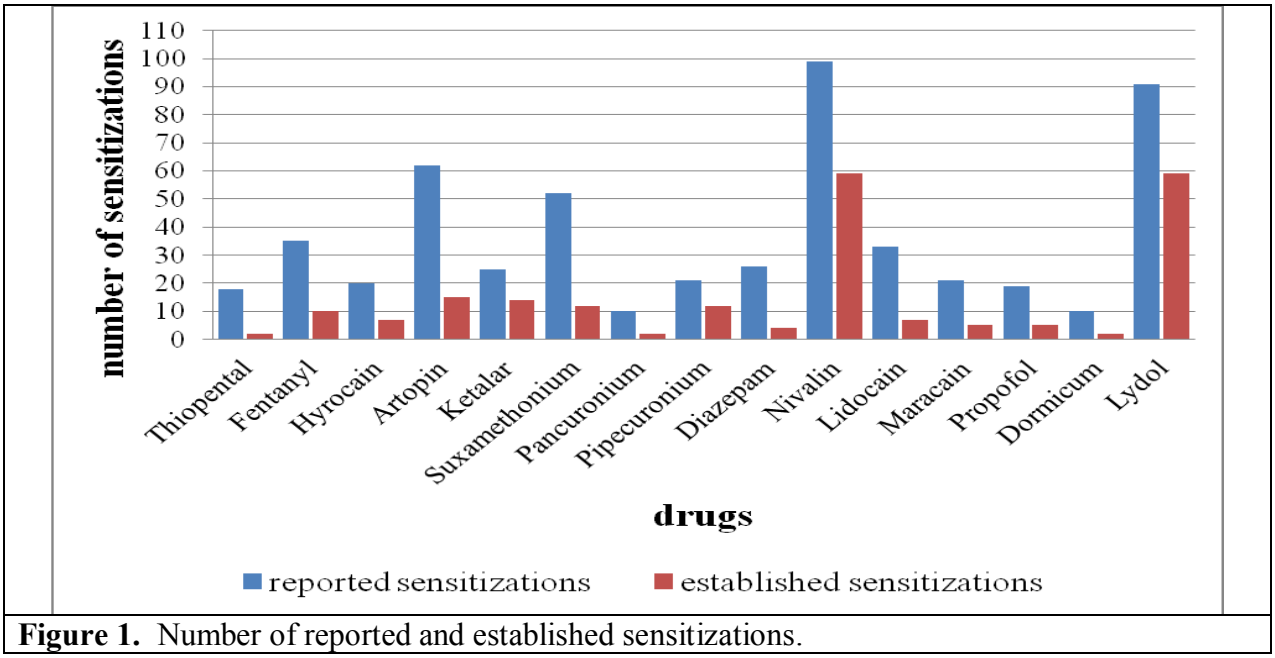

Figure 1. Number of reported and established sensitizations.

Discussion

Among the hypersensitivity reactions occurring during anesthesia, about 60% are mediated by an IgE dependent immunological mechanism (allergic reaction) (8). Skin test is the most commonly used procedure to confirm a sensitization to drugs

Considering anesthesia for members of the general population, it is not necessary to do a systemic screening for sensitivity to drugs (7). Patients at risk for anaphylaxis during anesthesia are those, who are allergic to one of the drugs or products likely to be administered during anesthesia and for which the diagnosis has been established by the previous allergy investigations (4). All patients included our study were admitted to hospital for operation. All of them had documented sensitization to drugs, used in anesthesiology practice.

A significant female predominance in sensitization and allergy to anesthetics are reported (5). We established that out of 356 patients, 277(69.38%) were women. Our study confirmed female predominance in sensitization.

In order to predict which patients might experience allergic drug reactions, it is essential to be able to determine the risk factor involved and the predictive value of the diagnostic tests (9)

Clinical history is of great importance to determine the patients at risk. A detailed history of all patients included in the study was taken with special attention to skin tests that previously had been done and for which patients had documents. As it became obvious all patients had scratch test previously done. Following recommendations for skin test procedures and performing SPT with recommended drug concentrations, our study confirmed sensitization in only 107 (30.06%) patients. A significant difference in sensitization to all tested drugs was established ($p < 0.05$). The reason for the significant difference could be explain with the use of scratch tests in previous drug evaluation which is poorly standardized. (10).

Conclusion.

The study established overdiagnosis in assessment of sensitization to drugs, used in anesthesiology practice. The overcome of overdiagnosis requires following the recommendations of International consensus on drug allergy. Prick test with drugs with standard concentrations as recommended by ENDA/ EAACI, carried out by highly skilled stuff can guarantee the proper diagnosis work up.

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