774 Is The Local Anaesthetics a Risk Factor of Anaphylaxis in Mastocytosis Patients?

P. Bonadonna[1]; E. Olivieri[1]; R. Zanotti[2]; I. Tanasi[2]; M. Oberti[2];F. Furci[3]

[1]Allergy Unit and Asthma Center, Hospital and University of Verona, Verona, Italy;

[2] Haematology Unit, Hospital and University of Verona, Verona, Italy;

[3] Allergy and Clinical Immunology Unit, University of Messina.

INTRODUCION: In the general population the incidence of real IgE-mediated reactions to LA is estimated to be <1% while the incidence of adverse reactions is much higher:Recently a Danish study carried out on 409 patients with a history of suspected allergic reaction to LA reports a real diagnosis of IgE-mediated reaction in none of the patients studied [1]. The real prevalence of LA hypersensitivity reactions in the general population is therefore overestimated. To confirm an allergic reaction to LA an allergological work-up is is necessary, which includes both the clinical history and skin tests.

Mastocytosis includes a heterogeneous group of clonal diseases, characterized by abnormal proliferation and infiltration of clonal mast cells in various tissues. Clinical presentation may vary from skin-limited (cutaneous mastocytosis) to systemic forms (systemic mastocytosis). (table 1)

Since surgical and anesthetic procedures, as well as other triggers, may lead to mast cells degranulation, these could be considered at risk in patients with clonal mast cell disorders [2] but the incidence of immediate reactions related to local anesthesia in patients with mastocytosis is unknown [3] and the are not enough data to support an increased risk for mastocytosis in patients with local anesthesia.

Table 1: WHO criteria for Systemic Mastocytosis.

The diagnosis of SM requires at least 1 major and 1 minor criteria, or 3 minor SM criteria.	
Major criterion	Presence of multifocal, dense mast cell infiltrates (>15 in aggregates) in bone marrow or extracutaneous organs
Minor criteria	• >25% mast cells spindle-shaped or with abnormal morphology in bone marrow or extracutaneous organs; • Detection of c-Kit point mutation at codon 816 in bone marrow, blood or extra cutaneous organs; • Mast cells that coexpress CD117 with CD2 and/or CD25, in bone marrow or extracuaneous organs; • Persistent increased serum total tryptase level (>20 ng/mL).

METHODS: Between 2012-2018, a total of 432 subjects with a median age of 52.9 years (range 17-86 years) underwent bone marrow biopsy after local anesthesia in suspicion of systemic mastocytosis (SM).

Patients were referred to our multidisciplinary group because of systemic reactions to Hymenoptera venom (n=243, 56.3%), maculopapular cutaneous mastocytosis (MPCM) (n=55, 12.8%), unexplained osteoporosis (n=44, 10.1%), drug or food allergy (n=34, 7.9%), symptoms due to mediator release (n=38, 8.8%), blood count abnormalities, hepatomegaly, splenomegaly or lymphadenopathy (n=12, 2.8%), systemic reactions to other insects bite (n=5, 1.1%), unexplained osteosclerosis (n=1, 0.2%).

In case of a positive history of local anesthetic allergy or multiple and severe drug allergy, an allergological work-up for LA allergy was performed before the procedure, including skin prick test, intradermal test, and subcutaneous provocation. All subjects received local anesthesia with lidocaine (n=406, 94%) or mepivacaine (n=26, 6%) before bone marrow biopsy.

Premedication with oral prednisone, diphenhydramine and ranitidine, was given only to those having marked mediator-related symptoms. After bone marrow evaluation, 252 of 432 patients (58%) were diagnosed with a clonal mast cell disorder)and 180 (42%) were found to be negative and used as control cohort in this study.

RESULTS :

The entire cohort included 432 subjects, of whom 252 patients with mastocytosis and 180 negative controls. The baseline "characteristics" of our study cohort is shown in table 2.

Parameter	Mastocytosis Group, N=252(100%)	Control Group, N=180 (100%)
Male/Female (Ratio)	158/94 (1.68)	88/92 (0.95)
Median Age	51.48	55.07
History of Local Anesthetics Allergy, No (%)	5/252 (2.0%)	7/180 (3.9%)
Lidocaine, No (%)	4/5 (80.0%)	2/7 (28.5%)
Mepivacaine, No (%)	1/5 (20.0%)	5/7 (71.4%)
History of Drug Allergy, No (%)	47 (18.6%)	52 (28.8%)
History of Food Allergy, No (%)	19 (7.5%)	11 (6.1%)

RESULTS : Among 252 patients with CMD, diagnosis were distributed as you see in table 3.

Table 3 : Distribution of diagnosis in the mastocytosis group (n=252, 100%)

	No (%)
Indolent systemic mastocytosis (ISM) without skin involvement	155 (61.5%)
Indolent systemic mastocytosis (ISM) with skin involvement	75 (29.8%)
Clonal Mast cell activation syndrome (CMAS)	9 (3.6%)
Cutaneous mastocytosis (CM)	6 (2.4%)
Systemic mastocytosis with an associated hematologic neoplasm (SM-AHN)	6 (2.4%)
Aggressive systemic mastocytosis (ASM)	1 (0.4%)

RESULTS: In the entire cohort of 432 patients, only 12 (2.8%) had a positive history for local anesthetic allergy, of whom 5 patients with indolent systemic mastocytosis and 7 controls.

Among 5 patients affected by mastocytosis, with positive history for LA allergy, four of them referred an adverse reaction to lidocaine and one to mepivacaine. Of seven controls, two of them referred an allergic reaction to lidocaine and five to mepivacaine. All of them underwent an allergological work-up before the procedure and were found to be negative for mepivacaine and lidocaine allergy tests. For precaution, patients with a history of LA allergy to lidocaine received mepivacaine and vice versa. Only one out of eleven received additional premedication. None of them experienced an adverse reaction during the procedure.

Among 432 subjects, 406 (94%) underwent bone marrow biopsy after lidocaine and 26 (6%) after mepivacaine local anesthesia. Of 26 subjects anesthetized using mepivacaine, 9 were diagnosed with indolent systemic mastocytosis and one with cutaneous mastocytosis without systemic involvement. Six of them also received steroids and antihistamine premedication because of severe mediator release symptoms. **Only one patient in the entire study cohort of 432 patients, with a negative history of LA allergy, developed a suspected allergic reaction to lidocaine during the procedure** : About 10 minutes after the administration of lidocaine, he complained discomfort and flushing, therfore the procedure was suspended. A blood pressure measurement showed severe hypotension. He rapidly recovered after intravenous hydrocortisone and antihistamine and he was monitored until resolution.

In our study, patients diagnosed with CMD who had a history of drug allergy had a higher probability to have a positive history for local anesthetics allergy (p=.046) Nevertheless, the only one patient who developed a systemic allergic reaction to lidocaine, during bone marrow biopsy, had a negative history whether for drugs or local anesthetic allergy. Moreover, among patients with CMD and drug allergy, we found a stronger association between history of antibiotics and LA allergy (p=.012).

CONCLUSION:

In our knowledge this is the first and larger study reporting on the safety of local anesthesia in patients affected by mastocytosis. Our study shows that local anesthesia must be considered safe even in patients with mast cell disorders, despite a positive history for drug or local anesthetics allergy or mediator release symptoms. Furthermore, in our cohort we did not find any significant association between a positive history for local anesthetics, drugs or food allergy and local anesthetics allergic reactions. For this reason, we believe that a positive history for drug, food or anesthetics allergy is not itself a risk factor for developing LA reactions.

According to our experience, we do not recommend premedication before local anesthesia, with the exception of patients with marked mediator release symptoms or with a history of severe drug allergy.

REFERENCES:

1. No cases of perioperative allergy to local anaesthetics in the Danish Anaesthesia Allergy Centre. Acta Anaesthesiol Scand 2017. 61: 149-155
2. Valent P, Akin C, Escribano L, Fodinger M, Hartmann K, Brockow K, et al. Standards and standardization in mastocytosis: consensus statements on diagnostics, treatment recommendations and response criteria. Eur J Clin Invest 2007;37:435-53.
3. Dewachter P, Castells MC, Hepner DL, Mouton-Faivre C. Perioperative management of patients with mastocytosis. Anesthesiology 2014;120:753-9