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321.COAGULATION AND FIBRINOLYSIS: BASIC AND TRANSLATIONAL

Real Word Data on Levels of Emicizumab and Their Correspondence with the Global Hemostatic Capacity and the Spontaneous Joint Bleeding in Patients on Emicizumab Prophylaxis

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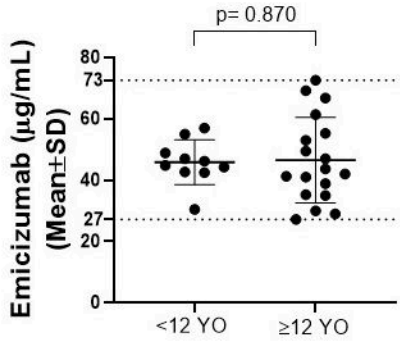
Introduction: Emicizumab has improved the management of patients with hemophilia A. However, few real-world data are available on drug plasma levels and their correspondence with global hemostatic capacity (GHC) and annualized spontaneous joint bleeding rate (ASJBR).
Aims: Evaluation of the correlation between emicizumab plasma levels, GHC and ASJBR in patients on emicizumab prophylaxis.
Methods: Multicenter, observational and cross-sectional study was performed in 4 Spanish hospitals. Emicizumab plasma levels and thrombin generation capacity (TGT, Genesia ®, Stago ®) of patients on emicizumab prophylaxis were determined in a central laboratory. Kinetics of clot formation was evaluated by rotational thromboelastometry (ROTEM ®, naTEM ® test, Werfen ®) in one center. Time on emicizumab prophylaxis and the number of spontaneous joint bleeds (SJB) was collected retrospectively using the clinical history. Results are expressed as median (25^{th}-75^{th} percentiles) or mean ± standard deviation depending on data distribution. A p-value < 0.05 was considered statistically significant.
Results: Twenty-eight patients were included: 18 aged ≥12 years (age= 20.1 [14.7-38.9] years old) (group 1) and 10 patients aged <12 years (age= 6.1 [3.2-8.9] years old) (group 2) (p< 0.001). Globally, emicizumab levels were 46.3 ± 11.9 mcg/mL and similar between both groups: 45.2 ± 13.1 mcg/mL (group 1) and 45.9 ± 7.3 mcg/mL (group 2) (p=0.870) (Figure 1). No correlation was detected between emicizumab levels and TGT or ROTEM ®. Compared with healthy controls, patients presented lower values of thrombin generation: Peak (% compared to controls) = 41.4 (33.3-53.0) % and endogenous thrombin potential (ETP%) = 54.9 (38.9-73.4) %. However, on the contrary, ROTEM ® showed a similar procoagulant profile (example: CT and CT+CFT; p>0.05) or even higher (example: lower CFT values in patients; p= 0.023) compared to healthy subjects (Table 1). Throughout a follow-up period of 57.0 (32.3-102.3) weeks, none of the patients presented SJB (ASJBR =0).
Conclusions: Emicizumab treatment provided excellent protection to patients throughout the study period. The wide interpatient variation on emicizumab plasma levels does not appear to have an impact on the development of SJB. TGT and ROTEM ® showed contradictory results: TGT describes lower thrombin generation capacity in patients compared to healthy controls, while ROTEM ® showed a similar or even higher procoagulant function in patients. Additional studies are required to explain these findings and their clinical significance.

Disclosures No relevant conflicts of interest to declare.

Figure 1: Plasma levels of emicizumab in patients aged < 12 years old and with age ≥ 12 years old (YO).



SD: standard deviation.

Table 1: TGT and ROTEM in patients and healthy controls. Peak% and ETP% refer to the percentage of peak and endogenous thrombin potential achieved in patients compared to that obtained in healthy controls. CT: Clotting time; CFT: Clot formation time.

Test	Parameter	Patients	Healthy Controls	p
TGT	Peak (%)	41.4 (33.3-53.0)	100%	< 0.001*
	ETP (%)	54.9 (38.9-73.4)	100%	< 0.001*
ROTEM® (naTEM®)	CT (s)	768 (695-861)	718 (680-836)	0.602
	CFT (s)	209 (163-309)	308 (203-331)	0.023*
	CT+CFT (s)	1028 (877-1115)	1028 (883-1212)	0.473

Figure 1

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