SYSTEMATIC COMPARISON OF DIFFERENT METHODS FOR THE MEASUREMENT OF C1 INHIBITOR ANTIGENIC CONCENTRATION

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Introduction: Hereditary angioedema (HAE) due to C1-inhibitor (C1-INH) deficiency is a potentially life-threatening rare disease caused by the decreased activity of C1-INH. In HAE type I decreased C1-INH activity is caused by the decreased production of C1-INH. In HAE type II patients the antigenic level of C1-INH is normal or increased with~~out~~ depressed inhibitory activity. The diagnosis can be established based on the measurement of the C1-INH antigenic concentration (C1-INHa) and the C1-INH functional activity (C1-INHf). Several methods are available to measure both C1-INHa and C1-INHf. In our study we aimed to compare measuring C1-INHa with radial immuno-diffusion (RID) and with ELISA.

Methods: RID have made with polyclonal anti-C1-INH antibody from Quidel (San Diego). To the in-house ELISA we used the same antibody from Quidel (San Diego), and the biotinylated Quidel's antibody as secondary antibody. Different dilutions of plasma derived human C1-INH (CSL Behring) was used as standards and to determine the measurable range. We compared C1-INHa tests in different sample types (serum, EDTA-, citrated-, hirudin plasma) taken from healthy volunteers.

Results: The measurable concentration in RID is 10000 fold higher than in ELISA. The linear range is longer in ELISA than in RID (2.1 Log vs. 1.5 Log). Interestingly, despite the superior sensitivity and linearity of ELISA, C1-INHa measure by ELISA was systematically 0.5 fold lower than measured by RID. There is a difference by the two methods according to the type of the sample (serum, EDTA-, citrated- or hirudin plasma) used in the measurements. In the RID method the C1-INHa levels detected from citrated plasma are lower than from the other sample types (average 0.86 fold), whereas in the case of ELISA this difference is more pronounced (average 0.68 fold). Matrix effect did not alter significantly the measurable C1-INHa levels tested by either methods, i.e. the same values were calculated when the samples were serially diluted.

Discussion: Despite the longer linear range and large sensitivity of ELISA method we can measure 2 fold higher C1-INHa levels with the RID assay. We can conclude that despite the differences we found both RID assay and ELISA method is feasible for measuring C1-INHa, however, it is important that the results given by the two methods cannot compare directly. All sample types is usable in both RID

assay and ELISA method, while C1-INHa levels measured from citrated plasma are lower than C1-INHa levels measured from the other sample type in both assays, the usage of citrated plasma is less proposed.