Prodromes and Attacks of Hereditary Angioedema

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Background: Hereditary Angioedema (HAE) is a rare genetic disorder, resulting from low levels or dysfunctional regulatory enzyme (C1-esterase Inhibitor, C1-INH). The main role of C1-INH is to control blood vessels permeability. The disorder is clinically presented by recurrent and almost unpredictable episodes of swelling in various organs and tissues. As a lifelong chronic illness, HAE has significant influence on daily activities and quality-of-life. Early manifestations (prodromes) have been observed in association with HAE attacks. Despite many reports by patients, up to present time there is lack of data about the prodrome definition by scientific measures. By our group was developed the new tool (the questionnaire based on Patient-reported Outcome measures) for detection and assessment of HAE prodromes. This instrument has shown its usefulness in evaluating prodromes and attacks and predicting an oncoming attack.

Objectives: To evaluate successive prodromes and attacks by a new HAE-specific instrument, and examine its associations .

Methods: The prospective study include 48 patients (mean age 33 years, SD ±16.4), with HAE reporting their experience with successive pairs of prodromes and attacks on four different occasions. Pre-defined domains (i.e. clusters of body locations) and scalable dimensions (i.e. severity, impairment, functionality) were assessed in each episode by an HAE-specific questionnaire. Statistical analysis included calculations of the differences and associations between prodromes and attacks, predictive validity, risk ratio (Chi-square tests with Fisher exact correction); and sensitivity/specificity of the prodrome-scales to foretell the occurrence of an attack (ROC curves).

Results: It was found significant differences between prodromes and attacks across all dimensions. By bi-variate Pearson's coefficient was revealed positive correlations for similar body clusters. Severity of prodromes was correlated with severity of attacks across all clusters, but most significantly in the urogenital cluster ($r = .574$, $p < .01$). Severity of pain in prodromes was correlated to severity of pain during attacks involving the extremities ($r = .291$, $p < .05$) and oropharynges ($r = .936$, $p < .01$). Impairment in prodromes was correlated with attacks in all locations, particularly in the abdomen ($r = .288$, $p < .05$) and facial ($r = .588$, $p < .05$). Functionality bore the most significant correlations. Impairment of daily activity during a prodrome was correlated with subsequent abdomen ($r = .366$, $p < .01$), facial ($r = .882$, $p < .01$), extremities ($r = .381$, $p < .05$) and oropharyngeal ($r = .790$, $p < .05$) attacks. The individuals who experienced a prodrome, have higher risk for attack in the abdomen (RR=2.30), urogenital (RR=16.39), facial (RR=2.94), extremities (RR=5.55) and oropharyngeal (RR=33.31) locations .

Conclusions: The results of our study support the probability of having an attack based on the occurrence of a prodrome. Assessment by HAE-specific questionnaire can be useful tool to alert patients to oncoming attacks and allow the deployment of therapeutic strategies for early attacks treatment.