Acta Derm Venereol 2015; 95: 225–226

SHORT COMMUNICATION

Health-related Quality of Life in Danish Patients with Hereditary Angioedema

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Accepted Mar 3, 2014; Epub ahead of print Mar 7, 2014

Hereditary angioedema (HAE) is a rare, but potentially life-threatening disease characterised by attacks of swellings. It is caused by a lack of functioning C1 esterase inhibitor (C1INH). The oedema is usually located to the face, extremities or abdominal mucosa, but may involve the larynx. Although rare, the laryngeal attacks are particularly dreaded due to the risk of asphyxiation. It is known that HAE can have substantial impact on health-related quality of life (HRQoL) (1, 2). Today, Danish HAE patients have access to several modalities of treatment including intravenously administered C1INH concentrate (3). Patients are offered training in self-injection if they suffer from frequent and/or severe attacks. The aim of this study was to investigate HRQoL in Danish HAE patients.

METHODS

The study was carried out in 2009 at the Danish HAE Comprehensive Care Centre, Odense University Hospital. Twenty-seven Danish HAE patients filled out The Short Form (36) Health Survey, version 2 (SF-36v2) and a clinical questionnaire. Patients were asked about number and locations of attacks within the last 6 months, age of onset, types of treatment and ability to do self-injection. Danish population norms for SF-36v2 were not available, it was recommended by the producers to compare to the US population norms (4). To examine if there was any correlation between disease severity and score in SF-36v2, a clinical severity score recently developed by Bygum et al. (5) was used. Patients were divided into 3 groups based on disease severity, and for each group median scores in SF-36v2 were calculated. We also examined whether scores in SF-36v2 were related to self-injection with C1INH concentrate by calculating median scores for the self-injecting and non-self-injecting subgroup, respectively.

RESULTS

Fig. 1 outlines the SF-36v2 mean score reported for 8 specific dimensions. In all dimensions but one, HAE patients rate equally to or higher than the general population. The relation between disease severity and median scores in SF-36v2 is illustrated with a box and whiskers plot (Fig. 2). In all dimensions there is no statistically significant difference in median score between the 3 severity groups ($p > 0.05$ in Kruskall-Wallis test). In the study, 25 patients had C1INH concentrate at home and 11 were able to do self-injection. In the dimension General health the self-injecting subgroup scored lower than the non-self-injecting subgroup (median 58 [39.3–67.8] versus median 77 [55.8–92.8], $p = 0.049$ in Mann Whitney U rank-sum test). Otherwise there was no difference between the 2 groups. Nor did we find any general correlation between scores in SF-36v2 and the number of attacks within the last 6 months (data not shown).

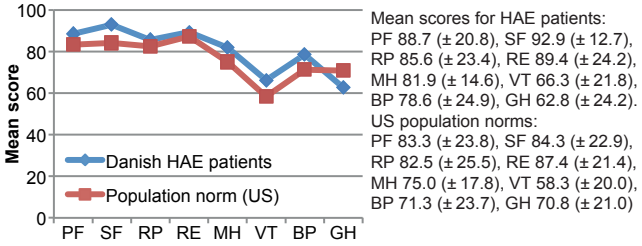

Fig. 1. Mean scores in SF-36v2 for Danish hereditary angioedema (HAE) patients vs. US population norms. PF: physical functioning; SF: social functioning; RP: role-physical; RE: role-emotional; MH: mental health; VT: vitality; BP: bodily pain; GH: general health.

DISCUSSION

It is noteworthy in our study that mean scores in SF-36v2 generally correspond well to the population norms. However, it has to be taken into consideration that the applied population norms were calculated in 1998 in the US. Also, the presented data are based on only 27 subjects and therefore have considerable statistical limitations. Still, such a cohort is sizeable for this rare condition.

Recently, a Brazilian study on HAE also based on SF-36v2 showed a significantly lower mean score in all dimensions (6). A possible explanation is the difference in treat-

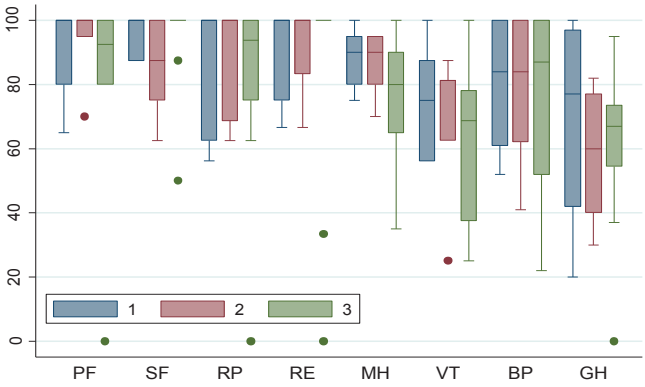

Fig. 2. Median scores in the 8 dimensions of SF-36v2 grouped by severity score. Group 1 has 4–6 points on the severity score, group 2 has 7–8 points and group 3 has 9–10 point. Single points are outliers. For abbreviations see Fig. 1.

ment options and health care systems between the countries. Danish patients are followed regularly at a specialist centre and have access to necessary medication and around the clock counselling. Treatment with C1INH concentrate was not approved in Brazil at the time of the study by Gomide et al. (6) and patients answering the questionnaire only had access to treatment with tranexamic acid or attenuated androgen (confirmed by correspondence with the authors). Both treatments are also used in Denmark, but to a lesser extent since newer treatments have better efficacy and fewer side effects. Twenty-five of the Danish patients had C1INH concentrate at home, and it has previously been shown that administration of C1INH concentrate is associated with QoL benefits (7–9). In our study we found no general difference in SF-36v2 scores between the self-injecting and non self-injecting patients. Only in the dimension General health there was a significantly lower score in the self-injecting subgroup. One reason for this could be that although home treatment has many benefits it is also a frequent reminder to the patients of their chronic disease. It should also be taken into consideration that training in self-injection is typically offered to patients with more frequent and/or severe attacks. This might influence their answers in the SF-36v2 questionnaire.

Recently, Caballero et al. (2) found that attack severity and frequency were significant predictors of HAE-related anxiety, whereas our study does not report any significant correlation between disease severity and HRQoL. Only a few HAE severity score systems exist and there does not seem to be consensus on which provides the best data (10, 11). It has previously been shown that early onset of symptoms is associated with a more severe cause of disease (2, 12). In our experience, age at onset combined with information on which areas of the body have been affected provide useful information about general disease severity, whereas need for long-term prophylaxis indicates a certain frequency and/or severity of attacks. The score developed by Bygum et al. (5), was initially developed to represent a cumulated disease score and not an actual activity score. But even when looking at current disease activity represented by number of attacks within the last 6 months, there is no general correlation to scores in SF-36v2. It seems that, as in many other diseases, the burden of illness in HAE is not only determined by disease severity. At least from this study we see that HAE patients with access to new therapies and regular visits at a specialist centre have SF-36v2 scores comparable to the general population. This emphasises the need for tailored patient care programs and a regular monitoring of QoL. Indeed, international HAE guidelines recommend that HRQoL should be measured annually (13). The SF-36v2 can be a useful tool for evaluating HRQoL for patients with various types of conditions, including HAE. However, it does not address the special characteristics and challenges of the disease. This could explain why we do not retrieve any clear correlation between disease severity and HRQoL, as seen in other studies. Thus, there is a need for disease-specific tools to fully cover all QoL-related areas affected by HAE. Weller et al. (14) recently published a QoL questionnaire for recurrent angioedema which includes but is not specific for HAE. An international HAE-specific QoL questionnaire is currently being developed in Spain, and the Danish HAE Comprehensive Care Centre has been participating in its validation and translation (15).

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