

Humanistic burden of hereditary angioedema: health-related quality of life, depression, productivity, and social consequences

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Hereditary angioedema (HAE) is a rare autosomal dominant disorder characterized by unpredictable acute attacks of swelling of the extremities, genitals, face, intestines, and larynx. This study assessed the health-related quality of life (HRQL) and economic burdens of HAE via a Web-based survey of US patients. The survey evaluated the impact of HAE on education, employment, social activity, and family life and included questions specifically about HAE experience and 3 standardized instruments: the 12-item Short Form (SF[®]-12) Health Survey, the Hamilton Depression Inventory–Short Form (HDI-SF), and the Work Productivity and Activity Impairment (WPAI) tool. It was approved by an institutional review board, and all participants provided informed consent. Of the 457 respondents (345 women, 112 men), 94% experienced an HAE attack within the prior 12 months (mean 26.9 episodes per year; mean duration of 61.3 hours). HAE patients reported significant decrements relative to historic population norms on the SF-12 Physical Component Summary (mean: 43.7 vs 49.6; $P < 0.0001$) and Mental Component Summary (mean: 42.6 vs 49.4; $P < 0.0001$). Patients with HAE had a higher mean HDI-SF score than population norms ($P < 0.001$); 42.5% of HAE patients scored > 8.5 on the HDI-SF, indicative of clinical depression. Productivity was markedly impaired in all WPAI categories, including 34% overall work impairment. Patients missed a mean of 3.3 work days due to their most recent HAE attack. Over-all, annual direct and indirect costs for an average HAE patient total US \$44,597; annual costs correlate with average attack severity (\$11,587 for mild attacks vs \$104,857 for severe attacks). Based on this study, HAE imparts significant economic and social burdens in terms of annual costs, HRQL decrements, increased depression, and reduced productivity.

Safety and efficacy of physician supervised self-Managed C1 Inhibitor individual replacement therapy

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C1 inhibitor (C1INH) has been shown to be a safe and effective treatment for HAE attacks. While patients typically receive acute attack treatment at a clinic or hospital, several studies have suggested that home infusion of C1INH is safe and provides a superior outcome when compared to treatment at a medical facility. To add insight into this issue, we compared the safety and efficacy of C1INH treatment between two groups: HAE patients receiving acute C1INH therapy in medical facilities and those receiving therapy at home under a physician supervised program. Thirty-nine subjects with severe HAE were enrolled: 18 received C1INH (Cinryze or Berinert) in the clinic and 21 received C1INH (Cetor) at home. All subjects received on-demand C1INH for acute HAE attacks. Subjects filled out an initial history questionnaire then completed weekly on-line questionnaires for 4 weeks. The total number of attacks during the study period was 120 in the clinic group (0.83/wk) and 171 in the home group (1.02/wk). The average (mean±SEM) patient-assessed severity of the attacks (1-10 scale, 10=worst) was significantly greater in the clinic group (5.82±0.25) compared to the home group (4.78±0.19; $p<0.005$). The total attack duration was also significantly longer in the clinic group (34.25± 2.49 hours) compared to the home group (8.02±1.04 hours; $p< 0.0001$). The clinic group experienced a higher mean monthly number of ER visits (0.21 vs 0.05), narcotic pain prescriptions (1.57 vs 0.77), days of work missed (2.4 vs 0.8), and nights of sleep disrupted (7.0 vs 2.2) than the home group. A higher percentage of injections were associated with bleeding (7.81% vs 0.58%), pain (7.21% vs 1.73%) or local infection (0.30% vs 0.00%) in the home group; although only one adverse event was deemed significant by the subject. In conclusion, physician supervised self-managed home C1INH therapy appears to be more effective than receiving C1INH in the clinic. There were more adverse events in the home infusion group, but the frequency was small and the severity minor. We propose that physician supervised self-managed C1INH therapy can enhance the well-being of many HAE patients.

Tolerability and efficacy of attenuated anabolic androgen therapy in 731 HAE patients

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17 α -alkylated androgens have been mainstays of long-term prophylactic HAE treatment for over 35 years. While the efficacy of androgens as an HAE therapy has been documented in a variety of studies, the safety of these agents has been controversial. Moreover, defining the tolerability and efficacy of androgen therapy becomes more important as alternative acute and prophylactic treatment options become available to physicians and their patients. 731 HAE patients were recruited to participate in a study regarding androgen use. 525 females and 206 males participated. The study was conducted using an on-line password protected questionnaire. 367 of the HAE patient respondents (49.5%) reported that they were currently taking an anabolic androgen for their HAE. Of these, 73% indicated that the therapy was moderately or completely effective. However, 87% indicated that they would reduce their androgen dose if another effective therapy was available. Indeed, 74% of these patients noted that they would probably or absolutely discontinue the medicine. Almost half of the patients currently taking androgens (48%) reported that side effects outweighed the medicine's benefit to a moderate or absolute degree. 197 of the respondents (26.5%) reported that they had previously taken androgens but discontinued the medicine. 80 percent of these patients cited ineffectiveness or significant side effects as the reason for stopping androgens. The 167 HAE patients (22.5%) who indicated that they had never taken androgens appear to represent a noteworthy unmet medical need. 75 percent said they have been to the emergency room for acute attack. In addition, 46 percent said that they regularly use narcotics to relieve pain associated with attacks for an average of 33 days a year. This large survey of HAE patient attitudes towards anabolic androgens reveals that a large majority consider the side effects to be substantial and troubling. It is striking that most of the patients surveyed have either stopped taking androgens or would be inclined to stop taking androgens if a better therapy becomes available. These results should be considered by physicians and insurers as the treatment landscape for HAE changes.