Living with HAE in Australia – the effect of prophylaxis on attack rate

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Aim

To determine the effect of HAE prophylactic therapies on HAE attack rates, patients' use of on- demand treatment (ODT), hospitalisation and days lost from work or school.

Background

HAE patients in Australia have access to effective ODT. Several prophylactic therapy options are available, however, access to the more modern effective therapies is very restricted. C1 INH therapies for prophylaxis require a patient to have eight or more attacks a month to qualify for subsidised access. While lanadelumab is a registered product in Australia it has not been listed as yet for reimbursement. A very small number of patients with a large disease burden have been granted access to it. This study was conducted to gather real time information about the burden of disease in our HAE patient cohort and in particular, to explore the effect of prophylactic therapy use on various outcome measures.

Methods

In this non-interventional, prospective, observational study in Australian patients with HAE, we sought to understand the various treatment pathways, impacts on individuals, and healthcare resource utilisation.

Enrolment and Participation

Patients with HAE C1-INH deficiency types 1 and 2, aged 12+ years, were recruited via specialist clinics and through the patient support group. With informed consent, baseline data on HAE status and therapy use was obtained. Weekly monitoring was conducted via SMS with two questions asked: Q1- "What HAE medications have you used this week?" and Q2- "Have you had an HAE attack this week?" Q1 determined the participant's observational medication category (on-demand or prophylaxis). An affirmative response to Q2 initiated a follow-up phone call to collect more detailed information about each attack. All data was entered into a database and then coded and analysed.

Statistical Analysis

The continuous variables were summarised as number of observations, mean, SD, minimum, median, and maximum. The categorical variables were summarised in tables of frequencies, and percentages. 95% CI have been reported if appropriate.

Results

The study was conducted between July 2019 and November 2020; 50 participants enrolled; 3 withdrew. Total observational time was >400 months with an average of 9.1 months (4 to 15.9 months) per subject. Table 1 summarises the total observational time and attack rates in the various medication categories. 457 attacks were reported by SMS. Detailed attack information was obtained in 338 attacks (74%).

Table 1. Patients within the ODT or various prophylaxis groups: total time observed and HAE attack rate in each category.

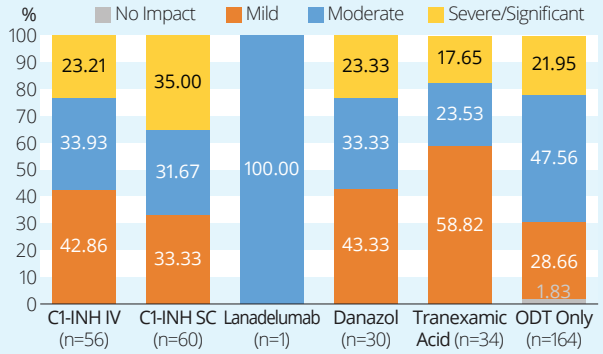
On Demand only or Prophylaxis Medication	Patients who had time within each category	Total Observed time (Months)	HAE Attacks (total)	Mean No. of HAE Attacks per month	95% CI for Mean
On Demand only*	21	145.3	234	1.89	(1.01, 2.76)
Danazol**	7	56.4	35	0.62	(0.10, 1.15)
Tranexamic Acid	4	32.4	37	1.05	(0.0, 2.10)
C1-INH conc IV #	15	71	56	1.31	(0.60, 2.02)
C1-INH conc SC#	15	69.8	67	1.17	(0.52, 1.82)
Lanadelumab##	4	22	1	0.16	(0.0, 0.68)
BCX7353^	1	4.2	27	6.37	0
TOTAL		401.2	457		

**Icatibant or C1-INH conc IV, **Became difficult to access in Australia during the study # Only available in Australia for patients having >8 attacks/month, ## Compassionate Access only, ^ Trial drug*

Attack severity

The severity of the HAE attacks was rated by the participant as either "No Impact / Mild / Moderate / Significant or Severe". Figure 1 shows the relative proportion of severity for each treatment group.

Figure 1. Attack severity grading for each treatment group expressed as a percentage of total number of attacks.
(n is the number of HAE attacks where this information was available).



On-demand treatment usage for acute attacks

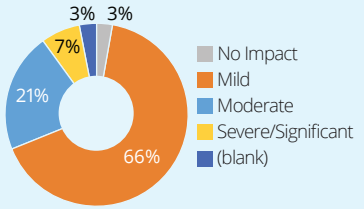
Detailed information regarding ODT usage was available for 338 acute attacks as follows:

- Icatibant: 236 doses used in 210 attacks. The majority used one dose (n=191) while in 14 attacks 2 doses were used and in 5 attacks 3 or more doses were used.
- C1-INH IV: used in 70 attacks either at home or in hospital, 500IU (n=3), 1000 IU (n=33), 1500IU (n=8) & 2000 IU (n=26) .
  - Combination of Icatibant and C1 INH IV used in 8 recorded attacks.
- 103 attacks were not treated with any ODT.

We explored the 103 non-treated attacks by severity rating shown in Figure 2.

Figure 2. Percentage of non-treated HAE attacks (n=103) by severity rating

23 (5%) of attacks required hospitalisation predominantly for facial/ throat swelling. These occurred in 9 participants with one participant recording 11 of 23 attacks.



Loss of productivity due to HAE attacks

Days lost from work or school as a result of an HAE attack was assessed where possible. 21 participants (44.7%) reported lost days due to HAE attacks. 58 attacks (17%) resulted in time off work/school. The total time lost was 85.5 days which ranged from 0.5 to 7 days per attack.

Figure 3. Number of HAE attacks which resulted in various days lost from work/school.

The majority of days lost were experienced by patients who were not on any prophylaxis and who relied on ODT only.

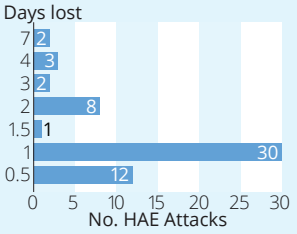
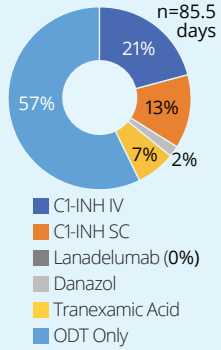


Figure 4. Total lost days by Treatment group.



Discussion

- This is a "first of its kind", long term, large observational study to determine humanistic impact & healthcare utilisation in a real world setting. Attack rate, severity and impact on work / school have been captured in real time without use of diaries, overcoming the reluctance of subjects to perform diary records.
- There were a number of factors throughout the study period that require discussion. Firstly, C1INH subcutaneous treatments became available after the study began so there were some patients who transitioned from IV to SC forms of prophylaxis. Secondly, Danazol became unavailable in Australia from early 2020 although other products could be obtained from overseas. This resulted in some patients moving from prophylaxis to ODT only and only those who had ≥ 8 attacks per month could be offered other options. Thirdly, this study overlapped the COVID 19 era so many people were working and studying from home for months of the study. Thus while some may have been very impacted by an attack, because they were not technically going out to work, patients did not register these times as days lost from work/school so the productivity data reported may in fact be an under-representation of the true work loss impact.
- Attack rate by treatment category shows the positive impact of prophylactic treatments and this is particularly so when one considers that only patients experiencing ≥ 8 attacks per month qualify for C1 NH prophylaxis and only a very small number have been given access to lanadelumab; these patients have failed to gain enough control on the C1 INH products.
- In this study, prophylactic therapy did not have an impact on reported HAE attack severity.
- Two thirds of attacks resulted in utilisation of acute therapy while no acute treatment was used in a third. Of those choosing not to treat, 66% rated their attack as mild leaving a third with greater severity choosing not to treat. This suggests that further education of patients on the wisdom of treating attacks is required.
- Productivity impact measured by days lost from work/school is substantial and almost certainly underestimated due to work / study from home rules during COVID-19 restrictions. Patients using ODT only show the greatest loss in productivity whereas using any prophylactic therapy results in improvement n this aspect of HAE burden.
- Further analysis is planned on Quality of Life impact, C1-INH dosing, COVID-19 impact and health economic resource costs.

Conclusion

This is a unique study format in HAE where data collection occurred each week without relying on diary records or patient long-term recall. When attacks occurred, phone follow-up allowed detailed information on resource usage and attack impact to be documented.

Data showed that HAE attacks can be frequent, debilitating and resource intensive. Prophylactic therapy was most impactful in prevention of loss of productivity. Further data analysis may help elucidate the optimal intervention strategy with effective modern prophylaxis therapies that are both patient and healthcare centric.

Declaration

Aesir Heath manage patient support programs for CSL Behring Australia. Dr Connie Katelaris has participated in Advisory Boards for CSL Behring Australia and Takeda. She has received institutional funding for clinical trials by CSL Behring, Biocryst and Takeda.

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