– LAY SUMMARIES –

SCIENTIFIC TRACK OF THE 2020 HAE VIRTUAL GLOBAL CONFERENCE

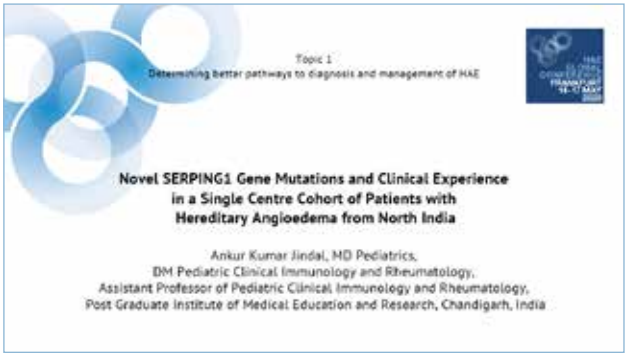
HAE GLOBAL CONFERENCE
FRANKFURT
14-17 MAY 2020

PRESENTATIONS FROM THE 2020 HAE VIRTUAL GLOBAL CONFERENCE

SCIENTIFIC TRACK

While the coronavirus COVID-19 pandemic prevented the planned version of the 2020 HAE Global Conference in Frankfurt, Germany, the "can-do" spirit of the HAE global community inspired transforming the widely anticipated bi-annual conference into an exciting virtual event.

At https://haei.org/gc2020/#scientific you will find the abstract book and video presentations from the Scientific Track under the topics "Determining better pathways to diagnosis and management of HAE" and "Creating a path to normalization of HAE patients' lives". The following are lay summaries of the presentations for the Scientific Track.



Novel SERPING1 Gene Mutations and Clinical Experience in a Single Centre Cohort of Patients with HAE from North India

Ankur Kumar Jindal[1], Anit Kaur[1], Amit Rawat[1], Dhrubajyoti Sharma[1], Himanshi Chaudhary[1], Anjani Gummadi[1], Sunil Dogra[2], Deepti Suri[1], Anju Gupta[1], Vikas Suri[3], Dipankar De[2], Vinay K[2], Varun Dhir[3], Surjit Singh[1]*

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BACKGROUND

There is a lack of information about the genetic profile and follow-up of people with HAE from developing countries. A group of clinicians in India examined the medical records of 52 HAE patients from 26 families, to understand more about the genetics of the condition and its management.

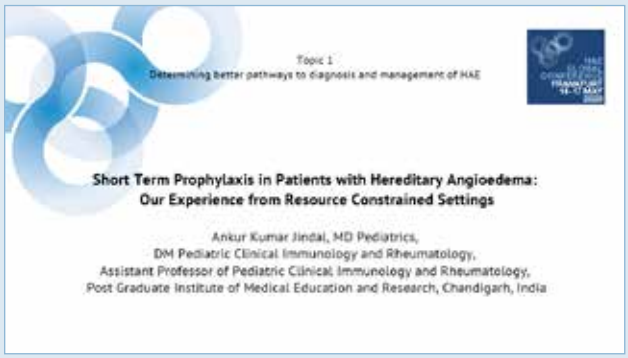
RESULTS

The authors found that the average time between onset of symptoms and a patient receiving a diagnosis was 11 years. In families where genetic sequencing had been conducted, just over half (11/21) had a mutation in the SERPING1 gene, which has been associated with the majority of cases of HAE.

In the management of their HAE, all patients received stanozolol or tranexamic acid, while acute, life-threatening, attacks were treated with plasma infusion. There was an average of over four-years of medical records per patient and none of the 52 patients died as a result of HAE.

WHAT DOES THIS MEAN FOR PATIENTS?

The study doctors conclude that this offers hope for people with HAE who live in resource-limited settings where C1-INH therapy is not available. The authors also question if the genetic background of patients with HAE in India may be different to other countries.



Short Term Prophylaxis in Patients with HAE: Our Experience from Resource Constrained Settings

Ankur Kumar Jindal[1], Ankita Singh[1], Himanshi Chaudhary[1], Anjani Gummadi[1], Anit Kaur[1], Manoj Jaiswal[2], Pooja Sikka[3], Amit Rawat[1], Deepti Suri[1], Anju Gupta[1], Surjit Singh[1]*

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BACKGROUND

Use of short-term medication to prevent attacks is necessary when patients with HAE are undergoing operations, as the surgical trauma could lead to an attack. A group of clinicians in India looked at options for short-term medication to prevent attacks of HAE in patients undergoing surgical procedures, when C1-INH therapy is not available.

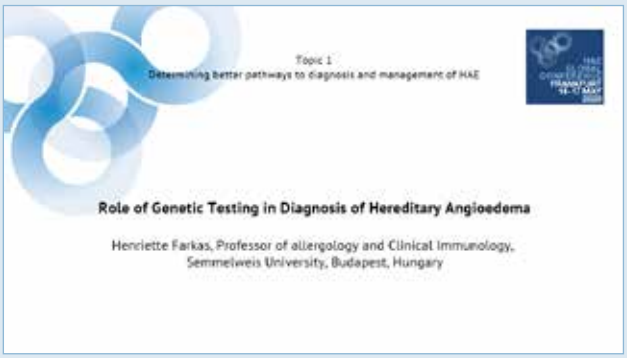
RESULTS

The authors report two case studies. The first was a nine-year old girl with HAE type 1, who was previously managed on tranexamic acid and stanozolol. Prior to dental surgery, the dose of stanozolol was doubled (0.5mg per day to 0.5mg twice a day). The patient also received infusions of fresh frozen plasma twice a day for two days before the surgery, and one dose during her operation. The authors report that the patient had a general anesthetic and a breathing tube inserted during an uneventful operation, and she suffered no HAE attacks.

The second patient case study was a 29-year old woman with HAE, previously treated with stanozolol and tranexamic acid. In two previous pregnancies, she took the medication and continued to experience attacks. These two pregnancies ended in the first three months and as a result she stopped taking medication. She became pregnant again and decided on a caesarean section. During the pregnancy she experienced no attacks. In preparation for the birth, she was given three units of fresh frozen plasma before the operation, along with 2mg stanozolol in the day before. Further units of fresh frozen plasma were given during the caesarean, and the stanozolol was continued for five days post operation. The operation was a success – she had an uneventful delivery and she had no episodes of angioedema.

WHAT DOES THIS MEAN FOR PATIENTS?

The study doctors conclude that short-term preventative treatment with fresh frozen plasma and stanozolol may be considered in patients with HAE undergoing operations, when C1-INH therapy is not available.



Role of Genetic Testing in Diagnosis of Hereditary Angioedema

Henriette Farkas[1], Edina Szabó[1], Anna Dóczi[1], Kinga Viktória Kohalmi[1], Lilian Varga1, Anastasios E. Germenis[2], Dorottya Csuka[1]

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BACKGROUND

Establishing a correct diagnosis of HAE could be crucial for a patient's prognosis and quality-of-life. Different types of testing can identify different types of HAE; complement testing can identify HAE with

C1-inhibitor deficiency whereas genetic testing is essential to accurately diagnose HAE with normal C1-inhibitor function. Genetic tests for SERPING1, factor XII (F12) and plasminogen (PLG) genes are available at the Hungarian Angioedema Reference Centre (HARC). Clinicians from specialist centers in Hungary and Greece used HARC to map the genetic mutation present in a group of HAE patients to help establish a correct diagnosis.

RESULTS

198 patients were followed-up at HARC. Following the genetic testing the authors found that 194 patients had hereditary C1-inhibitor deficiency (HC1-INH-def), two patients had factor XII (F12) gene mutation, whilst another two had a plasminogen (PLG) mutation. When patients were considered in family groups, 70 families were HC1-INH-def; one family with F12 and one family with PLG.

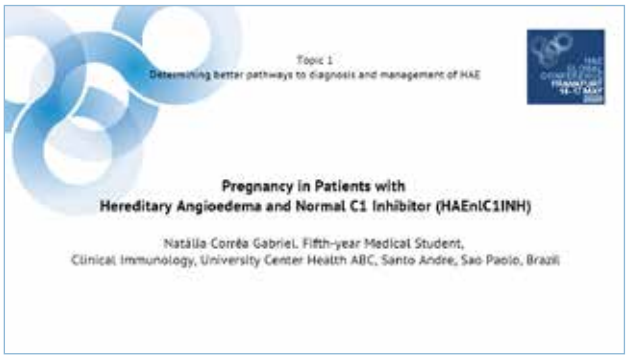
Of these family groups the authors saw from the genetic testing that;

- From the 70 HC1-INH def families, SERPING1 gene mutations were identified in 61 families
- In eight families with HC1-INH-def, mutation was not detected
- In a family with nC1-INH-HAE, F12 gene mutation was described which was a novel mutation
- A family with PLG-HAE was diagnosed

The authors also report that in five patients with C1-INH deficiency, genetic testing helped to establish a diagnosis (results from the complement testing was not clear) and in four patients they were able diagnose HC1-INH-def using blood taken from the umbilical cord of newborns.

WHAT DOES THIS MEAN FOR PATIENTS?

The increased use of genetic testing in cases of HAE will help distinguish between different types of the condition, especially in more complex cases where complement testing results aren't clear, or in infants where the immune system isn't yet fully formed.



Pregnancy in patients with HAE and Normal C1 Inhibitor (HAEnlC1INH)

Gabriel NC[1]; Martins RO[2]; Lobão NTM[3]; Campos RA[4]; Gonçalves RF[5]; Mansur E[6]; Ianni CO[5]; Ferraroni NR[7]; Grumach AS[1]

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BACKGROUND

Estrogen has been described as a trigger of attacks in patients with HAE with normal C1 inhibitor (HAE-nlC1-INH). Women are more likely to have symptoms, so there is concern that pregnancy may trigger the disease or lead to a worsening of the condition. There is a lack of information in this area and the authors present data from following the course of pregnancies in a number of women with HAE-nlC1-INH.

RESULTS

The study authors looked at the medical records of 26 Brazilian women with confirmed HAE-nlC1-INH. The average of the women now was 42.5 years and at the time of pregnancy, the average age of the women was 27.4 years.

These women had a total of 37 pregnancies. In 18 out of the 26 women, their first attacks were reported prior to being pregnant. In two out of the 26 women their first attack occurred during pregnancy, whilst in six out of the 26, the first attack was on average 2.5 years after a pregnancy.

When attacks did occur during pregnancy, they were most common in the 1st third of pregnancy (41.7%). 12.5% of attacks happened in the 2nd trimester, while 20.8% were in the 3rd trimester.

Fifteen women reported attacks before or during their pregnancy, with nine saying their condition got worse, and four reporting an improvement. One suggested no change and another one didn't respond.

Overall the authors found no difference in rates of miscarriage between women with HAE-nlC1-INH and those without the condition.

WHAT DOES THIS MEAN FOR PATIENTS?

Although data is limited, the authors conclude that pregnancy does not cause the onset of HAEnlC1INH, and that the impact of pregnancy on HAE attacks was temporary. Where patients may be concerned about long-term changes in their HAE due to or following pregnancy, the authors found that any change in attack rate – whether better or worse during pregnancy – did not continue long-term.

Next-Generation Sequencing (NGS) Provides More Information for Diagnosis Patients with HAE and Mixed Clinical Manifestations

Irina E. Guryanova[1], Valeria V. Pugacheva[1], Chiara Suffritti[2], Ekaterina A. Polyakova[1], Salivonchik Andrei[3], Mikhail V. Belevtsev[1], Sonia Caccia[4], Natalia E. Konoplya[1]*

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BACKGROUND

It is important to diagnose the acquired and hereditary forms of HAE accurately, as they are managed differently. The authors used the latest DNA sequencing technology (called next-generation sequencing or NGS) to investigate whether this technique could help establish an accurate diagnosis.

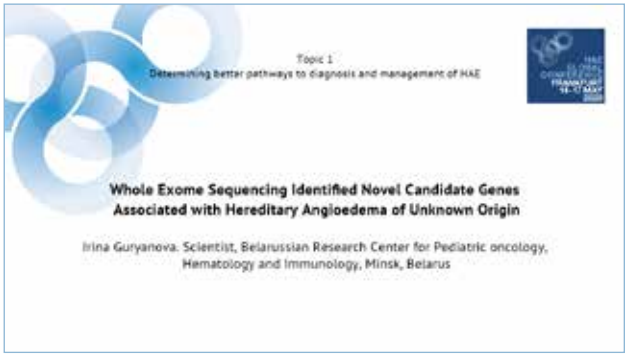
RESULTS

The authors investigated 257 patients who had angioedema without rash (urticaria), using a wide range of different tests using blood; C1-INH, C3c, C4, C1q, immunoglobulin E (gE), high molecular weight kininogen (HMWK) and antinuclear antibodies (ANA). In addition, the authors used NGS to sequence the SERPING1 gene, as well as more traditional Sanger sequencing.

Of all patients tested, 68 (26.5%) had genetically confirmed C1-INH-HAE, while 11 (4.3%) were found to have an acquired form of angioedema (IH-AAE). There were 39 patients (15.2%) where a specific trigger factor for their acquired angioedema could be identified, such as food, medication or environmental allergen. The authors also report on a family – not included in the numbers above - where an interesting and specific change was observed in the SERPING1 gene and had resulted in various forms of acquired angioedema being seen in family members.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors have provided a view on how NGS can be used in a clinical setting to help accurately diagnose a disease. Ultimately, accurate diagnosis ensures patients receive appropriate therapy which can improve quality of life.



Whole Exome Sequencing Identified Novel Candidate Genes Associated with HAE of Unknown Origin

Irina E. Guryanova[1], Vladislav R. Vertelco[1], Silvia Berra[2], Chiara Suffritti[3], Alexandr A. Migas[1], Ekaterina A. Polyakova[1], Andrei S. Babenka[4], Anastasiya V. Punko[1], Elena I. Lebedeva[5], Debora Parolin[2], Mikhail V. Belevtsev[1], Natalia E. Konoplya[1], Sonia Caccia[2]*

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BACKGROUND

Little is known about HAE of unknown origin (U-HAE), a condition which accounts for approximately 1% of all cases of HAE. By using the latest DNA sequencing technology, called next-generation sequencing (NGS) the authors hoped to better understand U-HAE.

RESULTS

The authors identified five individuals from two unrelated families who clinical and laboratory testing had shown signs of normal C1-INH-HAE. These patients were tested for 18 genes known to be associated with HAE, including FXII, PLG, ANGPT1 and KNG1, using NGS, but this sequencing didn't provide definitive results.

The authors then used a different form of genetic testing, called whole exome sequencing (WES), that is focused only on genes which allow the body to build proteins. Using this technique, a change on gene CPA3 was identified, which has never been described in relation to HAE. In the other family a variant of the ANGPT1 gene was identified, although this has already been associated with normal C1-INH-HAE.

WHAT DOES THIS MEAN FOR PATIENTS?

The identification of a potential new genetic change in patients with U-HAE may help with accurate diagnosis and treatment. However, this is early research in small numbers of patients. The authors will continue with this line of research and test all other members of the two families (both those with and without symptoms) to see if they share the genetic change or not. This would ensure that the genetic change can be confirmed as associated with HAE.

The FXII c.-4T>C Variant as a Disease Modifier in Patients with HAE due to the Thr309Lys FXII Mutation

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BACKGROUND

HAE due to mutations in the FXII gene can be complex to diagnose and manage, as the clinical symptoms can vary, and some people may have the mutated gene but not show symptoms of the condition. HAE due to the Thr309Lys mutation in FXII (HAE-FXII) mainly affects women, and in these patients, the symptoms can be greatly dependent on estrogen levels. The authors worked to better understand links between the c.-4T>C polymorphism – which has been recognized as influencing the variability of FXII plasma levels – and the severity of HAE symptoms.

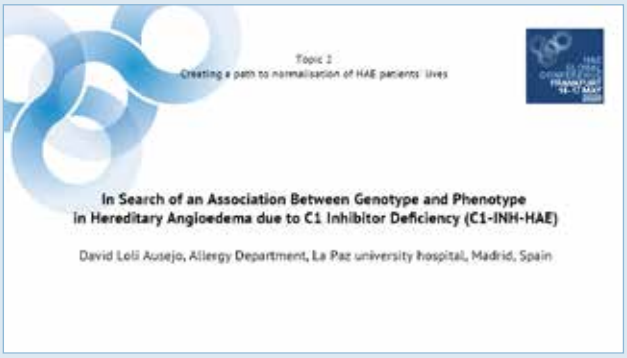
RESULTS

Thirty-nine non-related Spanish patients with HAE-FXII were investigated. The frequency that the c.-4T>C polymorphism occurred in the patients, along with their symptom severity, was assessed. In the patients, the authors report that the CC-homozygous (c.-4CC) was most common, with 71% having this form of the studied genotype. The patients with c.-4CC had significantly higher scores for severity of their HAE.

The authors also looked for evidence of association between the c.-4T>C polymorphism and the impact of estrogen levels or time to resolution of attacks but did not find any links.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that the c.-4T>C polymorphism can act as a genetic disease modifier which influenced the severity of symptoms of HAE-FXII in patients with the Thr309Lys mutation. They also conclude that due to its clinical impact and presence in many of the studied patients, c.-4T>C could be important for diagnosis.



In Search of an Association Between Genotype and Phenotype in HAE due to C1 Inhibitor Deficiency (C1-INH-HAE)

David Loli-Ausejo[1], Alberto López-Lera[2,3], Marina Lluncor[4], Elsa Phillips-Anglés[1], Rosario Cabañas[1,2], Teresa Caballero[1,2,3]

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BACKGROUND

HAE due to C1-inhibitor deficiency (C1-INH-HAE) is a caused by mutations affecting the SERPING1 gene. Bos et al have proposed a classification system for the mutations; class 0, class 1, class 2, class 2. These classes are not exclusive, so patients could have a mutation that belongs to more than one class. The authors wanted to investigate whether the observable characteristics of C1-INH-HAE could be simply aligned to or described by the classification system.

RESULTS

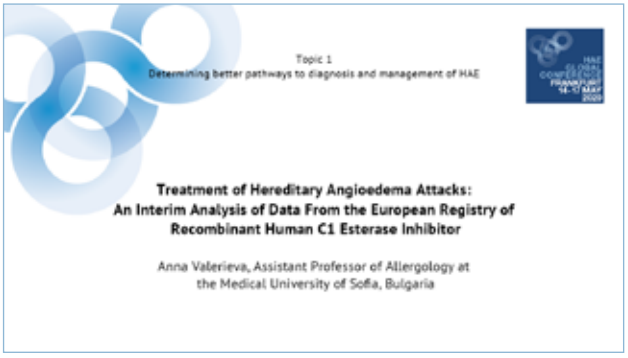
Eighty-eight adult patients were included in the analysis, of which 67 patients had mutations that could be classifiable according to the Bos et al system. Sixty-six patients corresponded to HAE type 1 and 1 patient to HAE type 2.

The authors found that there were variations in the characteristics and the mutation classifications. The mean age at onset of symptoms and at diagnosis were lower in patients with class 2 mutations. The highest average number of angioedema attacks was observed for patients with class 1 mutations. Similar C4 levels were found in patients in all mutation

classes. C1 inhibitor levels were higher in patients with class 1 mutations, and functional C1 inhibitor levels were higher in patients with class 2 mutations. A higher score for the HAE-Activity Score (HAE-AS) questionnaire (scale 0-30) was seen in patients with class 1 mutations.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that the results indicate that there are differences between the observable characteristics and the classes of SERPING1 gene mutations, but that much larger studies would be needed to confirm this.



Treatment of HAE Attacks: An Interim Analysis of Data from the European Registry of Recombinant Human C1 Esterase Inhibitor

Anna Valerieva[1], Maria T. Staevska[1], Vesna Grivcheva-Panovska[2], Milos Jesenak[3], Kinga Viktória Kőhalmi[4], Katarina Hrubiskova[5], Andrea Zanichelli[6], Luca Bellizzi[7], Anurag Relan[8], Roman Hakl[9], Henriette Farkas[4]

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BACKGROUND

An ongoing study, called a Registry, is following patients using recombinant human C1 esterase inhibitor (rhC1-INH) as a therapy for HAE. This study looks at attacks that patients have had, how well the therapy works for patients in their everyday lives, as well as any side effects of using this therapeutic option.

RESULTS

At the point that the authors analyzed the data, 85 patients with C1-inhibitor deficiency HAE (C1-INH-HAE) were enrolled in the Registry. Over an 8.5-year period, these patients experienced an average of 30 HAE attacks every year, totally 2,543 attacks and all the attacks were treated with rhC1-INH. Patients reported 96.9% of attacks were resolved by the use of rhC1-INH within four hours. Most HAE attacks (99.8%) only required one dose of rhC1-INH, with five HAE attacks being treated with a second dose.

The authors report that no hypersensitivity or blood clotting problems were reported, nor did patients report any serious drug-related adverse events.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that the data from 2,543 HAE attacks treated with rhC1-INH in everyday life, supports the safety and effectiveness of this form of therapy for HAE.

A Multicenter, Randomized, Double-Blind, Dose-Ranging Phase 2 Study Investigating the Efficacy, Pharmacokinetics (PK) and Safety of Prophylaxis with the Anti-Factor XIIa Monoclonal Antibody Garadacimab (CSL312) in Patients with HAE

DM. Cohn[1], BL. Zuraw[2], T. Craig[3], K. Bork[4], H. Feuersenger[5], I. Jacobs[6], I. Pragst[5]

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Veterans Affairs Healthcare, San Diego, California. 3) Allergy, Asthma, and Immunology, Department of Medicine and Pediatrics, Penn State University, Hershey, PA, USA. 4) Department of Dermatology, Johannes Gutenberg University Mainz, Mainz, Germany. 5) CSL Behring GmbH, Marburg, Germany. 6) CSL Behring, King of Prussia, PA, USA.

BACKGROUND

A potential new preventative therapy for HAE is being trialed in patients in a phase 2 study. This new therapy, which is not yet available for use, is called garadacimab. It works by inhibiting Factor XIIa, to prevent HAE attacks. This study looked at how garadacimab is processed in the body, as well as the optimal dose to maximize safety and efficacy in preventing attacks.

RESULTS

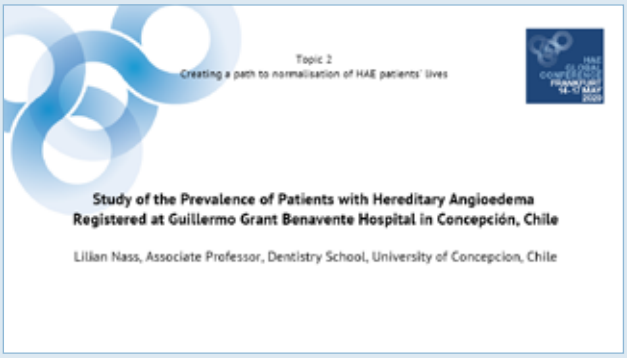
Thirty-two patients with C1-inhibitor deficiency HAE took part in this study. In order to be eligible, patients had to have had four or more HAE attacks in a consecutive two-month period (during the three months prior to joining the study), and at least two HAE attacks in any consecutive four-week period during the run-in period. Eligible adult patients were randomly assigned to receive 75mg, 200mg, or 600mg of garadacimab, or a dummy treatment (placebo) every four weeks during the first phase of treatment. After 13 weeks, a second treatment period saw all patients randomly receive either 200mg or 600mg of garadacimab for a further 44 weeks. Injections were given under the skin (subcutaneously) every four weeks.

Overall all doses of gardacimab reduced the mean number of HAE attacks; however, the 200mg and 600mg doses reduced the mean number of attacks by 98.94% and 90.50% respectively, which was not the result of chance (statistically significant, $P<0.001$).

All patients taking 200mg or 600mg of garadacimab reported side effects, however none were considered serious and none led to patients stopping the medication. The most common side effect of treatment was a mild to moderate reaction around the area of the injection.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that garadacimab is well-tolerated, and at the 200mg and 600mg doses was effective in reducing HAE attacks compared to placebo. This study provides the first clinical evidence of the role of Factor XIIa in C1-INH-HAE. The study is ongoing, and the results will inform the phase 3 study design to further evaluate the role of garadacimab in preventing attacks.



Study of the prevalence of patients with HAE registered at Guillermo Grant Benavente Hospital in Concepción, Chile

Dr. Lilian Nass, Dr. Gonzalo Espinoza, Dr. Matías Cisterna, Dra. María Nass, EU Caprice Sanhueza

Guillermo Grant Benavente Regional Hospital, Bronchopulmonary Department, Concepción, Chile. University of Concepción, Dentistry School, Department of Restorative Dentistry, Concepción, Chile.

BACKGROUND

Little is currently known about the prevalence and impact of HAE in the Bío – Bío and Nuble regions in Chile. The authors conducted a study of patients with Hereditary Angioedema at the Guillermo Grant Benavente Hospital – a Regional Hospital – in Conception, Chile to try and understand more.

RESULTS

Data was collected via review of clinical records of patients with HAE registered at the Regional Hospital. Patient consent was obtained for the review.

The preliminary results are for 17 HAE patients; of whom 11 are women and six are men. The patients have an average age of 39 years. The authors found patients had an average of 13 attacks over just under a year and a half (17 months); the highest number of attacks seen was 53, and the lowest number of attacks was one. One patient died as a result of an attack, which corresponded to 6% of the total number of patients.

WHAT DOES THIS MEAN FOR PATIENTS?

Thanks to the work of the authors, there is now a

better understanding of the prevalence and disease characteristics of the HAE patients in the Bío – Bío and Nuble regions in Chile. This information should support patients in terms of managing their attacks and increasing their quality of life.

Psychological Impact of HAE led to the Creation of the BITTEN Model of Trauma Informed Healthcare

Chrystal L. Lewis, PhD, RN1 & Jennifer Langhinrichsen-Rohling, PhD[2]

1) Institution: University of South Alabama, Department: Adult Health Nursing, Mobile, AL United States of America. 2) Institution: University of North Carolina Charlotte, Department: Psychological Science and Health Psychology, Charlotte, NC, United States of America.

BACKGROUND

People with HAE experience psychological impacts as a result of factors other than HAE. One possible cause for these impacts is institutional betrayal (IB). IB occurs when an individual's trust in an institution – such as healthcare providers – is betrayed through negative care or when expected care isn't delivered. HAE patients may experience healthcare system IB in different ways, for example:

1. having their symptoms of HAE dismissed or misdiagnosed
2. insurance denials
3. barriers accessing medication (for example due to an unfamiliarity with prescribing a particular rare medication, or the medication not being stocked) or
4. hospital system and structure failures due to unfamiliarity with HAE.

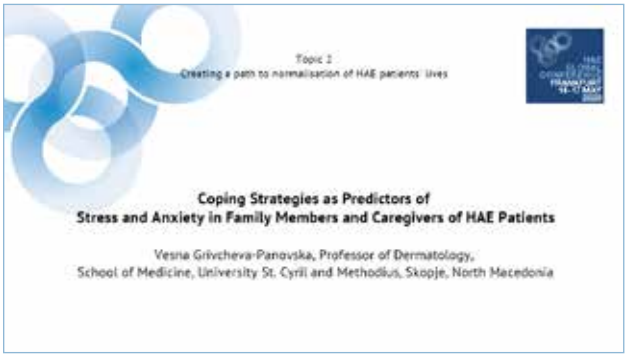
HAE patients are already at risk of experiencing medical trauma due to the severity and unpredictability of HAE attacks, and the authors identified that healthcare providers may not be prepared to address the impact of HAE attacks when combined with the psychological impact of any pre-existing IB. As a result, the authors developed a new model of care to help identify and appropriately address these challenges.

RESULTS

The authors were part of the team that created the BITTEN (Betrayal, Indicator for healthcare, Trauma history, Trust in provider, patient Expectations and Needs) Model of trauma informed care to provide a best practice framework for healthcare professionals. The BITTEN model helps healthcare professionals to look at past experiences to identify what the patient expectations of their current healthcare provision could be, and how patient needs for their healthcare experiences in the future can be addressed.

WHAT DOES THIS MEAN FOR PATIENTS?

The BITTEN Model helps healthcare professionals to understand that previous experiences may impact patient expectations of their current care, identify where these expectations are having a negative psychological impact and to respond appropriately with the ultimate aim of avoiding further negative healthcare experiences for the patient.



Coping strategies as predictors of stress and anxiety in family members and caregivers of HAE patients

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BACKGROUND

It is known that the unpredictability and fear of potentially life-threatening HAE attacks causes anxiety for patients, however patients' family members and caregivers (FM&C) can also experience anxiety as a result of fear of their loved ones having these attacks. It is also known that anxiety limits psychosocial functioning and has a strong impact on quality of life (QoL), however little is known about the coping strategies chosen by FM&C and their association with levels of anxiety experienced.

RESULTS

The authors report results from 178 FM&C of patients split into four groups:

- A1- 17 FM&C of HAE patients diagnosed less than (<) six months before the study start
- A2- 67 FM&C of HAE patients diagnosed more than (>) six months before the study start
- B1- 12 FM&C of patients with a severe food allergy which include angioedema symptoms diagnosed less than (<) six months before the study start
- B2- 82 FM&C of patients with a severe food allergy which include angioedema symptoms, diagnosed more than (>) six months before the study start

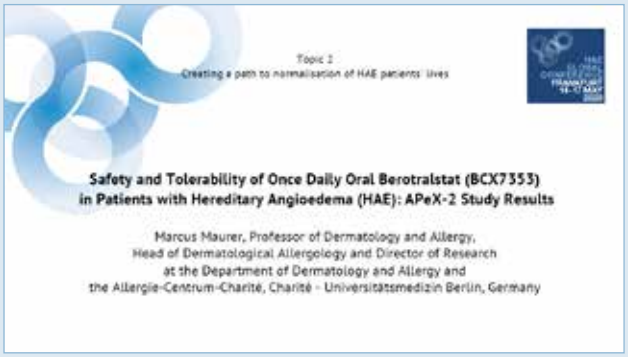
Group B was included in the study as a control group, and the authors explained that six months was chosen as the time frame to assess before and after, as studies have shown that this is the time needed to establish and build coping strategies. All participants underwent semi-structured interviews specialized for the purpose of the study using the Ways of Coping Questionnaire and the Hamilton Anxiety Rating Scale (HAM-A).

The authors found similarities in the groups where they were of similar timescales. In group A1 the coping strategy of confrontation was more pronounced (53%), and in group B1 confrontation was 42%. A high level of anxiety was diagnosed in group A1, where it was found that the coping strategies adopted, and high levels of anxiety, interfere QoL.

The most common strategies used post six months of diagnosis were planned problem solving (A2 & B2), seeking social support (A2), attitude (B2) and positive evaluation of the state (A2 & B2). Where these functional, positive and proactive coping styles were used, participants were found to have reduced levels of stress and anxiety related to the disease and its therapy.

WHAT DOES THIS STUDY MEAN FOR PATIENTS?

Using positive and proactive coping strategies can help reduce levels of anxiety and stress. This can lead to an increased following of healthcare professional advice and a positive effect on the overall health and QoL for the patient.



Safety and Tolerability of Once Daily Oral Berotralstat (BCX7353) in Patients with HAE: APeX-2 Study Results

Marcus Maurer[1], Jonathan Bernstein[2], Douglas Johnston[3], Aleena Banerji[4], Marc Riedl[5], Bruce Zuraw[5], Emel Aygören-Pürsün[6], Sandra C. Christiansen[5], Sylvia Dobo[7], Heather Iocca[7], Sharon Murray[7], Phil Collis[7], William R. Lumry[8] on behalf of the APeX-2 Investigators

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BACKGROUND

A potential new preventative therapy for HAE is being trialed in patients in a phase 3 study. This new therapy, which is not yet available for use, is called berotralstat and is a once a day oral pill. This phase 3 study investigates the safety and tolerability of this potential HAE therapy.

RESULTS

A total of 121 patients with HAE type 1 or 2, who had at least two confirmed attacks in the 56 days before treatment started, received either 110mg berotralstat or 150mg berotralstat, or a dummy pill for a period of 24 weeks. The number of side effects reported by

patients were collected, along with their severity and the likelihood that they were due to the new medication. In particular, the study examined any gastrointestinal side effects in detail.

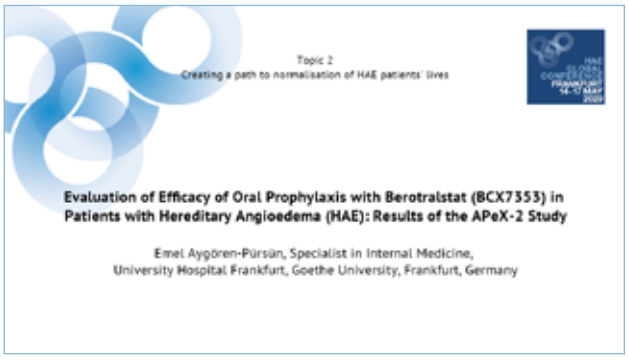
82.9% of patients taking 110mg berotralstat reported side effects. The proportion of patients taking 150mg berotralstat who reported side effects was 85.0%. In the placebo group (those taking the dummy pill) 76.9% of patients reported side effects.

The rate of side effects considered to be directly related to berotralstat were 41.5% in the 110mg group; 37.5% in the 150mg group and 33.3% in the placebo group. Four patients reported serious side effects; one from the group taking 110mg berotralstat and three taking placebo. Overall five patients stopped taking the therapy; three in the 110mg group, and one each in the 150mg group and placebo group.

The most common drug-related side effects were vomiting, diarrhea, abdominal pain and back pain. Gastrointestinal side effects were mostly mild, generally resolved without the need for medication and only led to one patient stopping treatment (one patient in 110mg group).

WHAT DOES THIS MEAN FOR PATIENTS?

Overall authors conclude that the study shows berotralstat is safe and generally well-tolerated at both 110mg and 150mg doses, with no serious drug-related side effects. The most common side effects were mild gastrointestinal problems. This study provides the largest in-patient clinical evidence for berotralstat to date, and results will inform applications to medicines approvers/ regulators in the future.



Evaluation of Efficacy of Oral Prophylaxis with Berotralstat (BCX7353) in Patients with HAE: Results of the APeX-2 Study

Emel Aygören-Pürsün[1], Sandra C. Christiansen[2], Marc Riedl[2], Bruce Zuraw[2], William R. Lumry[3], Douglas Johnston[4], Jonathan Bernstein[5], Marcus Maurer[6], Melanie Cornpropst[7], Sharon Murray[7], Eniko Nagy[7], William P. Sheridan[7], and Aleena Banerji[8] on behalf of the APeX-2 Investigators

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BACKGROUND

A potential new preventative therapy for HAE is being trialed in patients in a phase 3 study. This new therapy, which is not yet available for use, is called berotralstat and is a once a day oral pill. This study investigates how effective this potential HAE therapy is in patients.

RESULTS

A total of 121 patients with HAE type 1 or 2, who had at least two confirmed attacks in the 56 days before treatment started, received either 110mg berotralstat or 150mg berotralstat, or a dummy pill for a period of 24 weeks. Patients recorded HAE attacks in a diary and were asked to treat any attacks in accordance with their usual treatment plan. The authors were primarily examining the rate of confirmed HAE attacks during the 24 weeks of treatment, but also looked at the use of on-demand medication and the reduction in the number of confirmed HAE attacks compared to the rate before the trial started.

Presenting results from the 150mg group, the authors observed that patients taking 150mg berotralstat experienced 44.2% fewer attacks per month compared to the placebo group (those taking the dummy pill). In this group, more than half of patients (57.5%) experienced at least a 50% reduction in rates of HAE attacks, and half of patients (50%) experienced at least a 70% reduction in their rates of HAE attacks, both compared to HAE attack rates before the start of the trial.

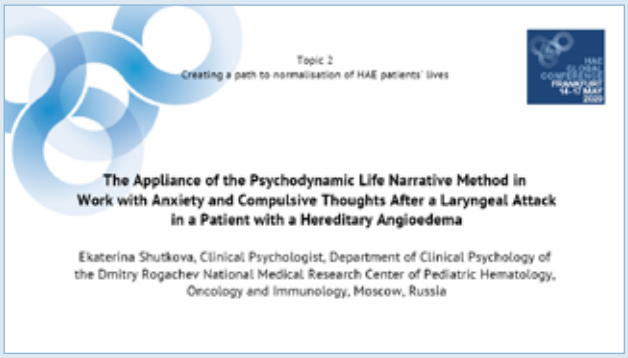
All patients taking berotralstat used less on-demand medication to manage HAE attacks. In the 150mg group this meant 1.5 fewer doses of on-demand medication per month.

Overall treatment with 150mg berotralstat led to a 44.2% reduction in the rate of HAE attacks; a 49.2% decrease in the rate of HAE attacks requiring treatment; and a 53.6% reduction in the use of on-demand medication, all when compared to placebo.

The authors report that the most common side effects of treatment were nasal congestion, nausea and vomiting.

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that HAE patients receiving berotralstat had fewer attacks, needed to treat fewer attacks and used less on-demand medication than those on placebo. This study provides the largest in-patient clinical evidence for berotralstat to date, and results will inform applications to medicines approvers/ regulators in the future.



The Appliance of the Psychodynamic Life Narrative Method in Work with Anxiety and Compulsive Thoughts after a Laryngeal Attack in a Patient with a HAE

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BACKGROUND

There is a link between mental health and the severity of HAE, with swellings of the upper airways being potentially life-threatening and therefore associated with high levels of patient anxiety. Psychological impact can also be a trigger for attacks. Methods to help patients deal with anxiety could be very valuable in improving management of HAE and lead to better quality of life for patients.

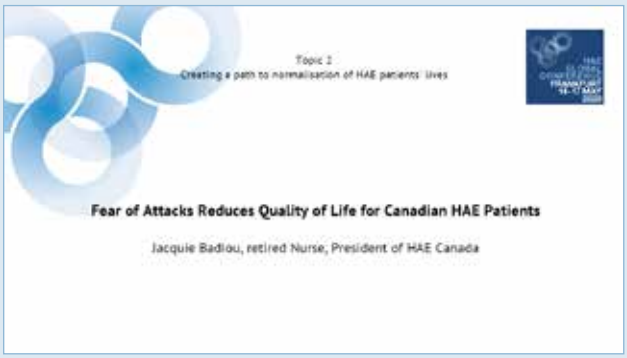
RESULTS

The authors report the case of a 37 woman with HAE, who had high levels of anxiety and compulsive thoughts related to having another HAE attack in her larynx (voice box in the throat). Her concerns were related to anxiety about death, a lack of control over her life, dependence on physicians and concern about being able to access medical help.

Using the psychodynamic life narrative method during three online consultations, psychologists helped the patient to place her anxieties in context of her current life circumstances. This helped reduce the amount of compulsive thoughts the patient had, and greatly reduced her anxiety.

WHAT DOES THIS MEAN FOR PATIENTS?

The author concludes that psychodynamic life narrative may be a promising way for HAE patients to lessen anxiety and reinforce a feeling of control. Further research on the psychodynamic life narrative could be promising to positively help anxiety and depression in HAE patients.



Fear of Attacks Reduces Quality of Life for Canadian HAE Patients

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BACKGROUND

Assessing the day-to-day experiences of HAE patients is important to understanding the impact of HAE on daily life. New prophylactic therapies offer the potential for a great reduction in HAE attacks, and the impact on daily life. HAE Canada wanted to assess the

challenges faced by HAE patients and caregivers as well as understand the impact that the availability of the newest prophylactic therapies has had for patients.

RESULTS

The authors report results from the first six questions, asked in two online surveys conducted in 2019.

The first survey looked at the challenges in daily life for HAE patients and included respondents who were treated with lanadelumab. In this survey, there were 73 respondents, 68 (92%) who were HAE patients and 6 (8%) caregivers. Respondents were asked how often that had attacks, and around one in three patients (29%) experienced attacks more than once a month and one in six patients experienced attacks more than once a week. Attacks most commonly occurred in the GI tract, the face and in the upper airway for patients. Three in four patients indicated that they feared having unpredictable and debilitating attacks. This resulted in more than half of respondents reporting generalized anxiety and also a desire for control of swelling and treatment plans.

Of the first survey respondent, eight had been treated with lanadelumab via participation in a clinical trial. Five patients considered it "extremely effective" in preventing attacks.

The second survey had 19 respondents and was designed to gather information about subcutaneous C1 inhibitor. Three respondents had received subcutaneous C1 inhibitor and all reported this to be "extremely effective".

In both surveys, reported side effects from patients taking lanedalumab or subcutaneous C1 inhibitor were "tolerable" to "very tolerable".

WHAT DOES THIS MEAN FOR PATIENTS?

The authors conclude that the fear of unpredictable, painful or life-threatening HAE attacks can lead to negative feelings and generalized anxiety. Patients report that the newest medications are effective in reducing attacks which could reduce the fear of attacks and so improve the quality of life of Canadian HAE patients.