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HAE. Hereditary Angioedema

NIHR BioResource – Rare Diseases study project

Lead Investigator: Dr Sorena Kiani

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Summary

Bradykinin mediated angioedema is a rare disease that is inherited in 80% of the patients but in 20% the genetic abnormality is not from the parents but appears sometime during the life of the individual (*de novo* mutations). It results in recurrent unexpected swellings in many anatomical locations such as hands, feet, face as well as tongue, throat or the gastrointestinal tract. These swellings can last for a few days and can be debilitating but they can also be life threatening if they involve the airways.

For some patients the main cause of this condition is known to be a mutation in the gene that codes for a regulatory protein called C1 esterase Inhibitor (CI-INH) but for others the faulty mechanism that can cause these abnormalities is not known. The other unknown is the reason for this disease to have a wide spectrum from very mild in some patients to very severe and debilitating in others. With patients who have the same mutation but different disease severity, the reason could be other genes that modify the disease.

By working with the NIHR BioResource we plan to identify the genetic causes of this group of conditions and the modifier genes that effect the severity. This could not only help with designing rational treatment for these patients but could also contribute to the understanding of the metabolic pathways that are involved in these diseases. This knowledge could be helpful in understanding many other conditions that involve these particular metabolic pathways.

Recruitment Criteria

Inclusion

All patients who have proven bradykinin (BK) mediated angioedema demonstrated either by:

1. Abnormal C1-INH levels and function
2. Abnormal BK production assay: increased cleaved high molecular weight kininogen product, increased kallikrein activity or any assay that can demonstrate an abnormality in production of BK that could lead to angioedema. (The latter includes biological assays that demonstrate increased breakdown of BK through assessment of the activities of Aminopeptidase P, Dipeptidyl Peptidase, Angiotensine-I converting enzyme and Carboxypeptidase N.)
3. Diagnosis of BK mediated angioedema based on the clinical criteria of angioedema with absence of urticarial or erythema and a failure to respond to regular use of high-dose antihistamines, or objective laboratory evidence of increased BK levels (increased production or reduced breakdown). (The final decision on whether the patient has BK mediated angioedema will be made based on the provided information by the principal investigators.)

Exclusion

Patients with angioedema who have responded to antihistamines and/or have associated urticarial rashes.