Children with HAE

DON’T PANIC

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Disclosures

• Shire
• CSL
• Pharming
Paediatric HAE

Symptom onset: mean 8-12 years

Bork K et al
University Hospitals Birmingham
When patients first developed symptoms

Presenter’s own data.
University Hospitals Birmingham
When do children first develop symptoms?

Presenter's own data.
Does my child have HAE?
How young can we diagnose correctly?
Parents are not believed or listened to by:

- Primary care
- Secondary care
- Relatives
• Age of testing is a matter of personal family choice

• Routine tests from 1 year

• Prior to 1 year blood tests MAY be less accurate
TIMECOURSE

Pain development

Longhurst & Cicardi, Lancet (2012); 379: 474-81
HAE patient with abdominal symptoms
What is HAE?
Factor XI

TRAUMA ➔

Factor Xla *

->

Factor XII

* ➔

Factor XIIa

* ➔

Autoactivation ➔

C1 ➔

Clα ➔

C4C2C3C5

* ➔

Plasmin ➔

Kallikrein ➔

Prekallikrein ➔

HMWK ➔

BRADYKININ

Vasodilation

Smooth muscle contraction

Oedema

Plasminogen ➔

Increased capillary permeability

Fluid extravasation

Oedema

C4a

C3a

C5a

C4b2a3b5b ➔

MAC

* = C1 esterase inhibitor - site of action
Impact on quality of life in adults and children

Adults

Children

Burden on the family

• Stress
• Earlier onset more severe disease?

• Do patients present with severe disease without previous mild / moderate symptoms
Individualised Management Plans

- A&E
- Home
- School
- Holiday
Individualised Management Plans

• Needs regular review as

  – changes in symptoms

  – And growing independence of the child.
Triggers

• Infected teeth and other foci of infection
• H. pylori
• Dental treatments
• Minor trauma
• Intubation for anaesthetics
• Puberty
• Physical or psychological stress
Treatment for children

- None: 25
- Tranexamic acid: 5
- Danazol: 1
- Stanozolol: 1
- Combination: 1
- Other: 1
Do all symptoms in Children with HAE need treatment?

- YES

- If does not cause problems
Children not just small adults

• Small
  – Difficult veins

• Scared
  – Children and adults

• Puberty
  – Progesterone only OCP

• School
Tranexamic acid inhibits factor XIIa and factor X, the initial steps in the coagulation cascade. Icatibant, on the other hand, inhibits bradykinin release, which is implicated in vasodilation, smooth muscle contraction, and increased capillary permeability.

- Tranexamic acid acts on factor XIIa and factor X.
- Icatibant acts on bradykinin.

Key points:
- Tranexamic acid inhibits factor XIIa and factor X.
- Icatibant inhibits bradykinin.
- Bradykinin leads to vasodilation, smooth muscle contraction, and increased capillary permeability.
- Increased capillary permeability leads to fluid extravasation and oedema.

* = C1 esterase inhibitor - site of action
Subcutaneous C1 inh?

(b) 3000 IU

C1-INH functional activity (%)

Time (days)
Subcutaneous C1 inh?
Icatibant

• Licensed for children over 2 years age

• Variable dose
Icatibant for children

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Dose (Injection Volume)</th>
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</thead>
<tbody>
<tr>
<td>12 kg to 25 kg</td>
<td>10 mg (1.0 ml)</td>
</tr>
<tr>
<td>26 kg to 40 kg</td>
<td>15 mg (1.5 ml)</td>
</tr>
<tr>
<td>41 kg to 50 kg</td>
<td>20 mg (2.0 ml)</td>
</tr>
<tr>
<td>51 kg to 65 kg</td>
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<td>&gt;65 kg</td>
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</table>
2) Screw the connector onto the pre-filled syringe.

3) Attach the graduated syringe to the other end of the connector ensuring that both connections fit securely.

Transferring the icatibant solution to the graduated syringe:

1) To start transfer of icatibant solution, push the pre-filled syringe plunger (on far left of below image).
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Potential problems with Icatibant in children

• Will parent use?

• Rarely used
  – Education
    • Re-education

• Expensive
  – Shelf life?

• Tolerated?
  – Post marketing surveillance
Future

• Icatibant for over 2 year olds

• Ruconest

• Monoclonal antibodies
  – Lanadelumab

• Oral Bradykinin / kallikrein inhibitors
Summary

• Children develop symptoms generally in the 2nd decade
Summary

• Children develop symptoms generally in the 2\textsuperscript{nd} decade
• Diagnosed after 1 year old
• Treatment for children with HAE?
  – Yes but far from perfect
  – But the future is bright
What families want

• To be believed
• Oral prophylaxis
• Oral treatments
• Once a year injection
Thank you

Any Questions?