Venous access in children undergoing ITI

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ITI

• ITI – different regiments
  – factor FVIII/FIX concentrates and/or by-passing agents administered i.v.
  – frequency from 3 x week to 2 x day

• sufficient and convenient venous access necessary!

I.v. routes

• peripheral vein
• central vein
  – central venous access devices
    • short time CVL
    • long time CVL
      – tunnelled
      – port-a-cath
• A-V fistula
Peripheral veins

- preferred if
  - large enough
  - sufficient number of available sites due to frequency of infusions
  - parents/caregivers are well trained
- low risk of
  - infection
  - thrombosis
- frequent changing of sites
  - to prevent skin and vessel wall scars

Peripheral veins

- 1 vein puncture a week
- inhibitors occurrence mainly in pre-school haemophilia patients
- 3-14 veins needed for ITI
  - usually not available in toddlers and pre-school boys
Peripheral veins

- painful venepuncture
- need for good compliance ("stillness")
- local anaesthetics can help
  EMLA cream 5%
  - (lidocaine+prilocaine) 1-2 hours prior puncture in occlusion

Peripheral veins

<table>
<thead>
<tr>
<th>Gauge</th>
<th>24</th>
<th>22</th>
<th>20</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>mm</td>
<td>0.7</td>
<td>0.9</td>
<td>1.1</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Vasofix inserted in a vein up to 72 hours

Peripherally Inserted Central Catheters

- higher risk of thrombosis
- lower risk of occlusion
- no data from haemophilia patients
Central Venous Access Devices

- external short term use
  - up to 4 weeks
  - emergency situations
  - after surgery

- external long-term use
  - tunnelled
    - Hickmann, Broviac
  - risk of infection
  - risk of self extraction
  - sterile techniques
  - regular flushing
    - saline, heparin
Central Venous Access Devices

- internal
  - ports (port-a-cath)

Central Venous Access Devices - Ports

- lower risk of infection
- longer life
- no risk of "self pulling"
- bathing possible

- puncture with needle required

CVAD infections

- exit site infection
- tunnel or pocket infection
- sepsis
CVADs: infection

- Pooled incidence of infection 0.66/1000 catheter days
- Factors associated with an increased risk of infection:
  - Presence of inhibitors
  - External lines
  - Age 2-6 years
  - Daily use

Reason for removal:
- 70% infection
- 4% thrombosis
  (Valentino et al, Haemophilia 2004)

CVAD infection = lower ITI success
  (ITI study)

81 CVADs, 3.36 years (0.22 - 9.44 years), Median age at first CVAD insertion 2.16 years (0.77-1414)

Overall incidence of confirmed CVAD-related bloodstream infection 0.42 per 1000 CVAD days,
Incidence of confirmed and suspected CVAD-related infection 0.60 per 1000 CVAD days

73.7% successfully treated iv ATB without CVAD removal
  (Yeoh et al, J Paediatr Child Health. 2013)

CVADs: thrombosis

- Even in haemophilia patients
- Asymptomatic:
  - On CVL
  - Mural
  - Complete occlusion
  - Risk of progression (VSC+VJI+VBC...)
- Locus of infection
  (Santagostino et al Blood Transfus 2008)

- 20 boys with haemophilia with total 27 CVADs
- MRI diagnosed DVT in 5 (25%), clinically silent, all inserted below 1 year
- No correlation between the duration or number of CVADs and DVT was detected. None of the patients had subjective symptoms of PTS
  (Ranta et al, Haemophilia 2012)

Management of port insertion

Kryštof, severe HA, HR IFVIII 35 BU/ml, 18 months

- Port-a-cath insertion for ITI, 12 kg
- rFVIII NovoSeven 1 mg = 83 ug/kg 2 mg = 166 ug/kg
- + paraaminobenzoic acid

- Graph showing NovoSeven mg over time with a total of 42 mg NovoSeven
Adrian, severe HA, HR IFVIII
Ports for ITI

<table>
<thead>
<tr>
<th>Port No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1000</td>
</tr>
<tr>
<td></td>
<td>100</td>
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</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>10</td>
<td>100</td>
</tr>
</tbody>
</table>

AV fistulas

- alternative to CVADs
- in haemophilia patients since 1999
  (Santagostino et al BJH 2003)
- surgeon experience
- non-dominant upper limb preferred

AV fistulas

- data from Italy, USA, Austria
- 1 month to maturation
  - dilatation and arterialisation of the vein
- 82% successful maturation
- duration of use 1-7 years (median 5 years)
AV fistulas

- Complications
  - Hematoma
  - Distal limb ischemia
  - Thrombosis of venous part
  - Loss of patency
  - Limb hypertrophy
  - Aneurysmatic dilatation

Summary

<table>
<thead>
<tr>
<th>Type</th>
<th>+</th>
<th>-</th>
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</thead>
<tbody>
<tr>
<td>PVPV</td>
<td>No external device</td>
<td>Not sufficient in small boys</td>
</tr>
<tr>
<td></td>
<td>No surgery, no special care</td>
<td>Haematoma post puncture</td>
</tr>
<tr>
<td>External CVL</td>
<td>No needle</td>
<td>Infection, thrombosis</td>
</tr>
<tr>
<td></td>
<td>Immediate use</td>
<td>Limited duration (year)</td>
</tr>
<tr>
<td></td>
<td>Percutaneous insertion</td>
<td>Self-displacement</td>
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<tr>
<td></td>
<td></td>
<td>Sterile techniques</td>
</tr>
<tr>
<td>Internal CVL</td>
<td>Longer duration (years)</td>
<td>Surgical insertion</td>
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<tr>
<td></td>
<td>No physical activity limits</td>
<td>Infection, thrombosis</td>
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<tr>
<td></td>
<td></td>
<td>Needles, skin erosion</td>
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<tr>
<td></td>
<td></td>
<td>Sterile techniques</td>
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<tr>
<td>AVF</td>
<td>No infection, no special care</td>
<td>Surgical construction</td>
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<tr>
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<td>Longer duration (years)</td>
<td>Delayed use</td>
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<tr>
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<td>No physical activity limits</td>
<td>AVF complications</td>
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Conclusions

- Adequate venous access is one of basic condition for successful ITI
- Peripheral vein is a best option
- CVAD or AV fistulas are possibilities
- Individual approach to patient
Future

- long acting drugs
- s.c. formulations
- p.o. formulations

Thank you for your attention