Recent and current research

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SSCAS meeting
RCPE
2nd September 2014
Outline: questions in acute stroke management & trials

- SOS: does routine O$_2$ improve outcome?
- ENOS: lower BP with GTN patch?
- ENOS: stop or continue BP lowering drugs?
- SYNTHESIS, IMS-3, MR-RESCUE – is endovascular treatment/clot retrieval better than IV thrombolysis?
- TICH-2 tranexamic acid for ICH?
- FOCUS does fluoxetine enhance recovery from stroke?
The Stroke Oxygen Supplementation (SO$_2$S) study:
A multi-centre, prospective, randomised, open, blinded-endpoint study of routine oxygen supplementation in the first 72 hours after stroke.

The SO$_2$S Collaborative Group

The Stroke Oxygen Supplementation Study is funded by the Health Technology Assessment Programme
Hypoxia after stroke

- Mean awake oxygen saturation in stroke patients 94.5%\(^1\)

- 63% have more than 5 minutes with SpO\(_2\)<96% in the first 48\(^2\)

- Oxygen desaturations < 90% are associated with

  - a doubling of mortality\(^3\)

  - a trebling of death and institutionalization\(^4\)

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Enrolled (n=8003)

Randomised (n=8003)

Allocated to continuous oxygen (n=2668)
- Assessed at 7 days (n=2641)
  - Lost to follow-up (n=10)
  - Withdrawn (n=17)
    - withdrawal of consent (n=10)
    - patient did not like treatment (n=5)
    - did not state reason (n=1)
    - other (n=1)
- Assessed at 90 days (n=2562)
  - Lost to follow-up (n=52)
  - Withdrawn (n=54)
    - withdrawal of consent (n=30)
    - patient did not like treatment (n=5)
    - patient left country (n=0)
    - did not state reason (n=6)
    - other (n=13)
- Analysed (n=2562)
  - Excluded from analysis (n=0)

Allocated to nocturnal oxygen (n=2667)
- Assessed at 7 days (n=2641)
  - Lost to follow-up (n=7)
  - Withdrawn (n=19)
    - withdrawal of consent (n=7)
    - patient did not like treatment (n=4)
    - did not state reason (n=1)
    - other (n=7)
- Assessed at 90 days (n=2558)
  - Lost to follow-up (n=49)
  - Withdrawn (n=60)
    - withdrawal of consent (n=30)
    - patient did not like treatment (n=5)
    - patient left country (n=1)
    - did not state reason (n=7)
    - other (n=17)
- Analysed (n=2558)
  - Excluded from analysis (n=0)

Allocated to control (n=2668)
- Assessed at 7 days (n=2654)
  - Lost to follow-up (n=10)
  - Withdrawn (n=4)
    - withdrawal of consent (n=2)
    - patient did not like treatment (n=0)
    - did not state reason (n=1)
    - other (n=1)
- Assessed at 90 days (n=2541)
  - Lost to follow-up (n=70)
  - Withdrawn (n=57)
    - withdrawal of consent (n=25)
    - patient did not like treatment (n=0)
    - patient left country (n=0)
    - did not state reason (n=7)
    - other (n=25)
- Analysed (n=2541)
  - Excluded from analysis (n=0)

Primary outcome available at 90 day follow-up in 95.7%
### Primary Outcome: mRS at 90 days

#### Oxygen vs. Control

<table>
<thead>
<tr>
<th>mRS</th>
<th>Combined oxygen</th>
<th>Control</th>
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<tbody>
<tr>
<td>N</td>
<td>%</td>
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<tr>
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<td>602</td>
<td>12%</td>
</tr>
<tr>
<td>1</td>
<td>1399</td>
<td>27%</td>
</tr>
<tr>
<td>2</td>
<td>635</td>
<td>12%</td>
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<tr>
<td>5</td>
<td>315</td>
<td>6%</td>
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<tr>
<td>6</td>
<td>495</td>
<td>10%</td>
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</tbody>
</table>

**Odds ratio for a better outcome with oxygen**

1.04 (95% CI 0.95, 1.13) p-value = 0.4
Conclusion

Routine low-dose oxygen supplementation in unselected stroke patients does not improve outcome

Broad inclusion criteria allowed a representative sample of patients to be recruited.
Efficacy of Nitric oxide in Stroke (ENOS) trial

Glyceryl Trinitrate (GTN) vs control
Stop vs continue antihypertensive drugs
Design

• International multicentre partial-factorial randomised controlled trial
• GTN (5 mg daily) vs No GTN (n=4011)
  – Patient-blinded; for 1 week
• Continue vs Stop pre-stroke BP drugs (n= 2095)
  – Open label; for 1 week
• Primary outcome: shift in modified Rankin Scale
  – Blinded central telephone assessment
• Recruitment July 2001-October 2013
• Final follow-up January 2014
Blood pressure GTN vs. control

\[ \Delta \quad 7.0 \quad 4.6 \quad 2.7 \quad 1.0 \quad 1.3 \quad 1.3 \quad 1.1 \quad \text{mmHg} \]

tachphylaxis
GTN vs control: Day 90 mRS

Ordinal analysis,
Common odds ratio
Adjusted OR 1.01 (0.90-1.13), p=0.83

Binary (mRS 3-6)
60.5% vs 61.3%
Adjusted OR 0.96 (0.83-1.12), p=0.64

No significant differences
Primary outcome: Subgroups

- Age
  - <=70
  - >70
- Sex
  - Female
  - Male
- Time to randomisation (hours)
  - <=6.0
  - 6.1-12.0
  - 12.1-24.0
  - 24.1-36
  - >36

![Graph showing odds ratio and 95% confidence intervals for different subgroups]
Stop vs continue BP drugs

Ordinal analyses,
Common odds ratio: Adjusted OR 1.05 (0.90-1.22), p=0.55

Binary (mRS 3-6) 65.6% vs 64.6%
Adjusted OR 0.94 (0.76-1.17), p=0.57

No significant differences
Systematic review of 5 randomised trials comparing endovascular therapy (ET) with iv rt-PA in acute ischaemic stroke

• 5 randomized trials 1197 patients
• There was no significant improvement in any of the outcomes in patients receiving ET compared with those receiving IV thrombolysis.
• CONCLUSION: Overall, ET is not superior to IV thrombolysis for acute ischemic strokes
• There is a need for further trials evaluating the role of ET

Ongoing trials of IVT vs endovascular

- MR Clean
- PISTE
- SWIFT prime
- THRACE
- ESCAPE
- REVASCAT
- And…. 
Conclusion for acute stroke

• Oxygen – no need for routine $O_2$
• BP lowering
  – GTN lowers BP (easy to use in non-swallowers), but no need to use routinely
  – Patients on BP lowering drugs can continue safely if needed during first few days after stroke
• Promote ongoing trials of
  – Intra-arterial clot retrieval
  – Tranexamic acid
  – Fluoxetine