Hyperbaric Oxygen (HBO) for Acute Carbon Monoxide Poisoning

Journal Club/ Grand Round Meeting in Administrative Medicine
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Physiological benefits
- Reduces COHb dissociation half-life
- Enhance dissociation of CO from cytochrome oxidase

Risks of HBO
- Hyperoxic seizures
- Barotrauma
- Claustrophobia

Evidence
- Case reports, uncontrolled observations, small, non-randomised unblinded studies, studies with incomplete assessment of outcomes
- RCTs: - 2 √ 2 X
  - All with risk of bias in study design

Evidence
- Problem: CO Poisoning
  - Intervention: Hyperbaric Oxygen treatment HBO
  - Comparison: Normobaric oxygen treatment CNBO
  - Outcome: Delayed neuropsychological sequelae

HBO or NBO for acute CO poisoning: a randomised controlled clinical trial
Scheinkestel et. al. MJA 1999; 170:203-210

Does early HBO reduce delay neuropsychological sequelae after CO poisoning?
Study design

RCT with neuropsychological tests and sham treatments in a multiplace hyperbaric chamber for patients treated with NBO

Patients

All during study period, exclude pregnant women, children, burns, refusing consent
Cluster randomisation

Intervention

➢ Daily 100-min with 100% oxygen in HB chamber: 60 min in HBO (2.8 atmosphere) and at l atmosphere for NBO for 3 days
➢ Continuous high flow oxygen in between

Outcome

Neuropsychological performance at completion and at one month (Based on 7 neuropsychological tests)

Neuropsychological sequelae

- Digit span subset of the Wechsler Adult Intelligence Scale
  - Digit span forward
  - Digit span backwards
  - Simple reaction time
  - Choice reaction time
  - Rey auditory verbal learning test
  - Short term free recall
  - Long term free recall

Results

All patients
HBO group requiring additional treatment 28%
NBO group requiring additional treatment 15%
OR 2.8 (1.3 – 6.2) P=0.01

Severely poisoned patients
HBO group requiring additional treatment 35%
NBO group requiring additional treatment 13%
OR 5.4 (2.0 – 14.8) P=0.001

Results

Average number of abnormal neuropsychological tests

<table>
<thead>
<tr>
<th></th>
<th>HBO</th>
<th>NBO</th>
<th>Difference in favour of HBO</th>
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<tbody>
<tr>
<td>All</td>
<td>3.4</td>
<td>2.7</td>
<td>-0.7 P=0.02</td>
</tr>
<tr>
<td>Severe</td>
<td>3.7</td>
<td>2.6</td>
<td>-1.1 P=0.008</td>
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Results

Poor outcome: persistent neurological sequelae (>2 abnormal test results)

<table>
<thead>
<tr>
<th></th>
<th>HBO</th>
<th>NBO</th>
<th>OR</th>
</tr>
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<tbody>
<tr>
<td>All</td>
<td>0.74</td>
<td>0.68</td>
<td>1.7(0.8-4) P=0.19</td>
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<tr>
<td>Severe</td>
<td>0.85</td>
<td>0.65</td>
<td>3.6 (1.1-11.9) P=0.03</td>
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</table>
Conclusion:

HBO did not benefit or may have worsened the outcome

Critical Review

1. Patients randomised?
   Yes: cluster randomisation

2. Was randomisation concealed?
   Yes: for patients, investigator and clinical psychologists
   No: for nurses and technicians

3. Were patient analysed in the groups to which they were randomised?
   Yes: Analyses was intention-to-treat

4. Were patient in treatment and control groups similar?
   Yes: similar to severely of exposure, duration until treatment
   Unusually high proportion (73%) of severely exposed suicide attempts with concomitant drugs and alcohol ingestion

Critical Review

1. At 1 month only 46% patient available
What are the results?

1. How large was the treatment effect?
   For PNS at discharge OR 3.6 (95% CI 1.1 – 11.9) P=0.03 in favor of NBO

2. How precise was the treatment effect?
   At CI 1.1, there would actually be little clinically important difference

3. PNS difference statistical significant?
   We are measuring “poor outcome” based on a subset of tests

How can we apply the results to our patient care?

1. Study patients similar to ours?
   Skewed towards suicide and severe co-exposure. Time to treatment > 7 hours

2. Were all patient–important outcomes considered?
   No. Dropout rate >50%, no conclusion can be drawn on delayed neurological sequelae

3. Are likely benefits worth potential harm & cost?
   9% HBO minor side effect HBO. would not benefit in preventing PNS as compared to NBO

HBO for acute CO poisoning

Weaver et. al. NEJM 2002; 347(14):1057-1067

Design: RCT, equal proportions to 3 chamber sessions with 24 hour period
   ¾ 3 HBO treatment sessions
   ¾ One NBO + 2 sessions of normal-baric room air
   ¾ Neuropsychological tests: after chamber session 1 and 3, 2 weeks, 6 month, 12 month
   ¾ Neuropsychological test: 6 subtests
Results- study stopped after interim analysis because HBO judged to be efficacious by the investigator

- Cognitive sequelae at six weeks
  - HBO 19/76 25% unadjusted OR 0.39
  - NBO 35/76 46% P=0.007

(P value of <0.05, Bonferroni’s correction used of the six neuropsychological subtests with level of significance=0.008: 0.05/6)
Bonferroni correction needed to adjust for multiple statistical comparisons / subgroup analysis

Adjustment for cerebellar dysfunction and stratification variables

- Adjusted OR 0.45 95% CI 0.22 – 0.92 P=0.03

Should we take this study as evidence for HBO?

Cerebellar dysfunction before treatment

Occurrence of cognitive sequelae

- OR 5.71
- 95% CI (1.69 – 19.31)
- P = 0.005

- HBO 4%
- NBO 15% P=0.03

Outcome:

No statistical significant after adjustment of cerebellar dysfunction and when Bonferroni’s correction is applied

Conclusion

- Current evidence comparing the efficacy of HBO and NBO has considerable limitations in study design and analysis and the results are inconsistent
- The evidence is insufficient for recommending definitive indications for HBO in CO poisoning