Hypoxemia post Liver-Transplantation for Hepatopulmonary Syndrome

HS Jeffrey Man
University Health Network and Mount Sinai Hospital
Keenan Research Centre at the Li Ka Shing Knowledge Institute,
St. Michael’s Hospital
University of Toronto
Goals

1) To define severe hypoxemia post liver-transplant for hepatopulmonary syndrome (HPS)
   - Identify a population who may need specialized management strategies

2) To propose an algorithm for management of post-transplant hypoxemia
Hepatopulmonary syndrome (HPS)

- 10-32% of patients with cirrhosis

Triad of:

1) liver dysfunction or portal hypertension
2) Intrapulmonary vascular dilatations
   - Contrast echocardiography or lung-perfuson scanning (brain shunt fraction >6% macroaggregated albumin)
3) Abnormal gas exchange (pO2 < 80mmHg or A-a gradient ≤ 15)
HEPATOMASULMONARY SYNDROME

Healthy alveolus

Intrapulmonary vascular dilatation
Potential mechanisms in the development of hepatopulmonary syndrome

Liver Transplantation for HPS

The only known effective treatment for HPS

Outcome is comparable to liver transplantation without HPS

Shunt reversal and corresponding improvement in gas exchange occurs in nearly 100% of LT survivors

Potential mechanisms of postoperative hypoxemia

Abrupt change in the vascular mediators entering the lung from hepatic effluent

Remodelling and impaired vasoconstriction of dilated HPS vessels such that normal pulmonary vessels may vasoconstrict disproportionately

Results in further increase in flow through dilated HPS vessels and worsening VQ mismatch and diffusion-perfusion defect
Defining severe hypoxemia in HPS post-liver transplantation (LT)

To:

1) Better estimate the prevalence (current and future studies)
2) Better understand the outcome
3) Identify patients at risk
4) Identify a therapeutic trigger for salvage treatment aimed at HPS-related hypoxemia
Defining severe hypoxemia in HPS post-liver transplantation

- Literature search: Included all case series that described post-LT complications in sufficient detail – 27 reports

- Found: No consistent definition

- Used the most commonly applied definition (19/27 reports)

- Defined as: hypoxemia requiring FiO2 1.0 to maintain O₂ sat ≥ 85% and out of proportion to other concurrent lung process

Nayyar et al. Liver Transplantation 2014; 20: 182-190
Prevalence and outcomes of severe post-liver transplantation hypoxemia

• Prevalence 12% (25/209 cases)

• Mortality 45%, leading cause of death in this group (68% of deaths)
  o 1 year mortality post-LT all comers 17% and for HPS 18%

• 81% reported onset by post-op day 3
  o 44% reported immediate post-op onset and 100% in our own case series

Nayyar et al. Liver Transplantation 2014; 20: 182-190
Who is at risk of severe hypoxemia post-LT?

• At risk – those with worse pathology pre-liver transplant
  o Patients with PaO2 < 50mmHg at risk of severe hypoxemia (20% vs 6% without)
  o Those with macroaggregated albumin shunt fraction > 20% (28% vs 4% without)

• Reinforces the importance of early liver transplantation
  o Hypoxemia is progressive in HPS (5-13mmHg/year decrease PaO₂)

• Those that survived period of severe hypoxemia had resolution of hypoxemia
  o Value of using salvage therapy as bridge to recovery

Nayyar et al. Liver Transplantation 2014; 20: 182-190
Goals of medical management

1) Mitigate early mortality

2) maintain oxygenation for long enough for post-transplant reversal of HPS pathology
Management options for severe hypoxemia in hepatopulmonary syndrome

• In general, the aim is to reduce blood flow through intrapulmonary vascular dilatations

• Management options include:
  o Trendelenburg positioning (1 pt)
  o Inhaled epoprostenol (4 pts) or inhaled nitric oxide (19 pts)
  o IV Methylene blue (10 pts)
  o Combined inhaled nitric oxide with IV methylene blue (2 pts)
  o Embolization of abnormal pulmonary vessels (2 pts)
  o Extracorporeal life support (3 pts)
TREATMENT: POSITIONING

Normal positioning

Trendelenburg positioning
TREATMENT: INHALED PULMONARY VASODILATOR

Healthy alveolus

Intrapulmonary vascular dilatation

Inhaled pulmonary vasodilator

Inhaled pulmonary vasodilator
TREATMENT: METHYLENE BLUE
Inhaled vasodilator + intravenous methylene blue

- Inhaled vasodilator preferentially vasodilates normal vessels in well-ventilated areas

- IV Methylene blue leads to vasoconstriction of intrapulmonary vascular dilations, where there is more blood flow, and may be relatively poorly ventilated
Embolization of lower lobar pulmonary vessels
Extracorporeal life support

• **Goal:**
  - Sustain tissue oxygenation until intrapulmonary vascular dilatations begin to reverse and pulmonary gas exchange improves

• **Caveat:**
  - Unpredictable time to resolution, so recommended if SaO₂ < 80% or end-organ dysfunction from hypoxemia
Algorithm

- Trigger: $O_2$ saturation $< 85\%$ despite $FiO_2$ of 1.0 for at least 1 hour with PEEP $\geq 10$mmHg

- Response to therapy defined as: change in $PaO_2/FiO_2$ ratio $\geq 20\%$ (30 min for all therapies except methylene blue which is 5 hours)
Severe posttransplant hypoxemia is defined as a saturation of <85%, for ≥1 hour despite an FIO₂ of 100% with a PEEP of ≥10 mm Hg¹

These patients should generally be kept dry to avoid pulmonary edema, which can compound hypoxemia related to intrapulmonary shunt

However, DO₂ should be maintained with hgb ≥ 100 and sufficient cardiac output for a normal SVO₂ (low SVO₂ has a disproportional effect on SaO₂ due to intrapulmonary shunt)

If other causes (e.g. pneumonia) contributing to hypoxemia, consider alternative ventilatory strategies as appropriate (e.g. HFOV)¹

---

**Trendelenburg Positioning²‡**

Response

Severe hypoxemia persists or recurs - Add:

**Inhaled Epoprostenol¹³ ‡**

No response - replace with:

**Inhaled Nitric Oxide³-⁶‡**

No response - add:

**Methylene Blue⁺⁷⁻⁹**

(3mg/kg IV dose X 1)

Response

Change to reverse Trendelenburg whenever using Methylene Blue

Discontinue Inhaled Epoprostenol Or Nitric Oxide¹⁰

---

**Maintain Minimum Dose for Response‡**

Response

Severe hypoxemia persists or recurs - Add:

**Re-start Inhaled Epoprostenol† Or Nitric Oxide¹⁰ and maintain Methylene Blue‡**

3mg/kg IV q2h

---

**Embolization of Abnormal Pulmonary Vessels¹¹⁻¹³**

And/Or

**Extracorporeal Membrane Oxidation¹⁴** (if patient meets ECLS criteria)

---

Summary: Severe Hypoxemia post – liver transplantation for HPS

- Defined as: hypoxemia requiring FiO2 1.0 to maintain O₂ sat ≥ 85% and out of proportion to other concurrent lung process.

- Affects 12% of HPS patients post liver transplant and is associated with a high mortality of 45%.

- Those that survive early severe hypoxemia will have resolution of HPS pathology.

- Management strategies target the specific pathology of HPS.
Thank you

• Samir Gupta – Hepatopulmonary Syndrome Program
  o GuptaS@smh.ca
• Dhruv Nayyar – Medical Student
• John Granton – Lung Transplant Program/ Critical Care
• Les Lilly – Liver Transplant Program