DOXYCYCLINE INHIBITS HEMORRHAGIC SHOCK INDUCED FLUID LEAK AND MICROVASCULAR ENDOTHELIAL DERANGEMENTS

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Nothing to Disclose
Hemorrhage

• Treatment:
  • Stop the bleeding and fill the tank

• But is it that simple...
Hemorrhagic Shock

Bench-to-bedside review: Latest results in hemorrhagic shock
Angele MK, Schneider CP, Chaudry IH - Crit Care (2008)
Vessel Permeability

Sham

0 minutes
30 minutes
60 minutes

HS
On a microscopic level, the Adherens Junction...
Matrix metalloproteinases

• Degrade ECM
• Degrade AJ proteins
ROS (Reactive Oxygen Species)

- Increase vascular permeability
- Mechanism not fully understood

![Chemical structures of ROS components: Oxygen (O₂), Superoxide anion (O₂⁻), Peroxide (O₂⁻²), Hydrogen Peroxide (H₂O₂), Hydroxyl radical (·OH), Hydroxyl ion (OH⁻).]
Doxycycline

Anti MMP and ROS outside HS

• AAA Aziz 2007
• HTN/CV disease Castro 2013
• Re-absorptive bone disease Franco 2011
• Trichiasis Li 2013
• Leukemia Wang 2015
• Burn Stagg 2013
Hypothesis

- HS
- MMP
- ROS

Fluid Leak
Serum Collected for in vitro experiments

Sham

HS
Experiments

- Rat Lung Microvascular Endothelial Cells

- 4 Groups:
  - Sham
  - HS
  - Sham + doxycycline (0.2ug/ml)
  - HS + doxycycline (0.2ug/ml)
Permeability
**Permeability**

- **Sham**
- **HS**
- **Sham + Doxycycline**
- **HS + Doxycycline**

* Sham vs HS, p<0.05
§ HS vs HS Doxycycline, p<0.05
ROS Formation Assay
**ROS Formation**

- **Sham**
- **HS**
- **Sham + Doxycycline**
- **HS + Doxycycline**

* Sham vs HS, p<0.05
§ HS vs HS Doxycycline, p<0.05
Adherens Junctions

- Cells stained for
  - β-Catenin
  - F-Actin
Adherens Junctions

Staining for β-Catenin

Sham

HS

Sham + Doxycycline

HS + Doxycycline
Adherens Junctions
Staining for f-Actin

Sham

Sham + Doxycycline

HS

HS + Doxycycline
Discussion

- HS
  - Increases vascular permeability
  - Increases permeability
  - Increases ROS formation
  - Damages adherens junctions
- Doxycycline attenuates changes in vitro
What’s next?

• Assay MMP-9 levels
• Examine Doxycycline in vivo
• And beyond…