PERSPECTIVES IN AORTIC TREATMENT

CYTOSORB THERAPY: CONTROLLING THE HYPERINFLAMMATION DURING AND POST CPB
Disclosure

Speaker name:

.....................Dr. Karl Traeger..........................................................

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

☐ I do not have any potential conflict of interest

- No surgical skills
- Intensivist
Cardio-Pulmonary-Bypass (CPB) as a paradigm of an inflammatory insult.

Time (days / weeks)

Pro-Inflammation

Anti-Inflammation

Organ failure

death

recovery

TOXIC

INSULT
Proinflammatory response
Excessive Inflammation causing collateral damage (tissue injury)
... Thus, vascular leakage caused by IL-6 transsignaling (resulting in tissue edema and hypoxia) represents a valuable novel target for pharmaceutical intervention and basic science ...
Overwhelming SIRS post CPB
SIRS - the systemic inflammatory response syndrome after cardiac operations

• Pathophysiology
  – Inflammatory stimuli
  – Surface contact
  – Inflammatory cytokine release
  – DAMPs

• Clinical symptoms
  – Hypotension
  – Vasoplegia
  – Capillary leakage
  – Pulmonary Dysfunction
  – Renal Dysfunction
  – MODS

• Therapeutic approaches
  – MECC (minimalized extracorporeal circulation)
  – Hemofiltration during CPB
  – Steroids
  – Catecholamines
  – Vasopressin
  – Hemoadsorption
Strategies to manage overwhelming SIRS post CPB

- Prophylaxis
- Preemptive treatment

**Treatment (ICU)**
- Catecholamines
- Steroids
- Vasopressin
- Fluids
- Organ support therapy

**Cytokine elimination**
Cytokines in the systemic inflammatory response syndrome: a review
Controlling cytokine storm during SIRS and SEPSIS by **ADSORPTION** (CytoSorb)

**Efficacy**
- Effective in decreasing elevated cytokine levels

**CE Registration (Europe)**
- First registered cytokine adsorber in Europe

**Safety**
- Safety by high biocompatibility (ISO 10993)

**Simple Use**
- Simple integration in CRRT circuits
- Whole blood hemoperfusion

**Fast Setup and Easy Handling**
- Compatibility with standard CRRT devices

**Reimbursement**
- OPS-Code 8-856, ZE 2014-09
Polymer-Technology: Bead Adsorber (Polystyrene-divinyl-copolymer)

- 300ml cartridge with „Bead“ design
- HighTech-Polymer
- Size selectivity < 55kD
- Low flow resistance
- 120ml volume
- Prefilled with NaCl solution
- Gamma sterilized, 3 yrs storable
Configuration and structure

Valenti, I “Characterization of a Novel Sorbent Polymer for the Treatment of Sepsis” 2008

CytoSorb™ Beads

Electron microscopic view of internal structure
Adsorber surface

Membrane filter

CytoSorb® Absorber

ca. 2 qm

>40.000qmqm
Controlling cytokine storm in the cardiosurgical patient

- **Preemptive approach**
  - During CPB

- **Therapeutic approach**
  - Adjunctive therapy postoperative / ICU
CytoSorb Treatment in SIRS post CPB

- Effects on cytokine levels?
Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series
Träger K et al., Int J Artif Organs 2016; 39: 141

IL-6 levels

IL-8 levels

Karl Träger, Daniel Fritzler, Guenther Fischer, Jannert Schröder, Christian Skrabal, Andreas Habold, Helmut Reinelt

(Head of Cardiac Anesthesiology, University Hospital Ulm, Ulm, Germany)
CytoSorb Treatment in SIRS post CPB

- Clinical effects?
Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series
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Epinephrine

Norepinephrine

Cardiac index

MAP
Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series
Träger K et al., Int J Artif Organs 2016; 39: 141

Lactate

Base excess

Baseline  Post CytoSorb  24h post CytoSorb
Adsorptive blood purification for control of inflammation triggered organ dysfunction

Effects of hemadsorption with CytoSorb in postoperative severe SIRS und Sepsis

• Reduction of increased cytokine levels
• Positive hemodynamic effects
• Reduced catecholamine need
• Metabolic stabilization
Controlling cytokine storm in the cardiosurgical patient

- **Preemptive approach**

- During CPB

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**STUDY PROTOCOL**

**RECCAS - REmoval of Cytokines during CArdiac Surgery: study protocol for a randomised controlled trial**

Andreas Baumann¹, Dirk Buchwald², Thorsten Annecke³, Martin Helm³, André van den Berg⁴, Jürgen Meier⁵, Steffen Breitenseher⁶, Wolfgang Walther⁵, Christian Kreyder⁵, Manuel Kudsk⁶, Gerhard Müller⁵, Christoph J. Hohenhaus⁴

Baumann et al. Trials (2016) 17:137
„Collateral“ elimination effects with CytoSorb treatment

Elimination of

- Free hemoglobin
  Dimer 32 kDa
  Tetramer 65 kDa
- Myoglobin 17 kDa
- Bilirubin 8 kDa
- Toxins
- ?
CONCLUSION
CytoSorb treatment options in cardiac surgery

**Therapeutic approach**
- SIRS post CPB
- Septic shock
- Severe reperfusion
- Severe hemolysis
- ...

**Preemptive approach**
- Acute endocarditis
- Local infections
- Complex and long lasting surgery
- Long CPB and x-clamp time
- Re-Do
CytoSorb Registry
http://www.cytosorb-registry.org

Koordination:
ZKS, Zentrum für Klinische Studien am Universitätsklinikum Jena
(Prof. Dr. F.M. Brunckhorst)
Future perspective: CytoSorb treatment in cardiac surgery and intensive care medicine...