The effect of vasopressor dosing strategy on microcirculatory perfusion in preclinical models of sepsis: a systematic review

Tyler James¹, Homer Yang², Francois Lamontagne³, Emilie Belley-Cote⁴, Frederick D’Aragon⁴, Duncan J. Stewart⁵,⁶, Manoj M Lalu²
¹University of Ottawa, Faculty of Medicine, ²Department of Anesthesiology The Ottawa Hospital Research Institute, ³Department of Médecine, Université de Sherbrooke, ⁴Department of Clinical Epidemiology and Biostatistics, McMaster University, ⁵Regenerative Medicine Program, The Ottawa Hospital Research Institute, ⁶Department of Cell and Molecular Medicine

Introduction

Sepsis
- Sepsis is a systemic inflammatory response due to an infection¹
- The inflammatory response can cause excessive vasodilation contributing to a decreased blood pressure³
- If blood pressure is decreased drastically it can dangerously lower organ perfusion resulting in septic shock and vital organ failure⁴
- The mortality rate of septic shock is 20-30% and it is the number one cause of death in critically ill patients²,⁵

The Role of Vasopressors in Septic Shock
- Vasopressors are drugs used clinically to counteract vasodilation and increase blood pressure⁶
- Along with antibiotic treatment and fluid resuscitation, vasopressors are nearly universally used to treat septic shock by increasing blood pressure⁷
- Surviving Sepsis Clinical Practice Guidelines suggest titrating vasopressor dose to achieve a mean arterial blood pressure ≥ 65 mm Hg, however this recommendation has weak supporting evidence⁸
- Interestingly, increasing blood pressure using vasopressors induces vasconstriction, which may reduce microcirculatory blood flow to vital organs and cause harm
- By using invasive methods to measure microcirculatory flow, preclinical studies of sepsis offer a unique opportunity to investigate the effects of vasopressors on microcirculation
- To date, a comprehensive summary of vasopressor dosing strategies on microcirculatory flow in sepsis has not been completed

Objective

We propose a systematic review and meta-analysis to answer the following question:
In preclinical studies using animal models of sepsis, what is the effect of different vasopressor dosing strategies on microcirculatory flow?

Methods

Electronic Search: EMBASE Classic, EMBASE, Ovid Medline, In-Process & Other Non-Indexed Citations and Ovid Medline, BIOSIS, manual review of bibliographies of selected articles (inception to February 2015)

Study Design: Eligible studies include only controlled comparison (randomized, nonrandomized and quasi-randomized) animal experiments

Population: Preclinical in vivo models that mimic the pathophysiology of human patients with septic shock

Intervention: At least two different vasopressor dosing strategies

Primary Outcome: Microcirculatory perfusion measured by the following methods:
- Tonometry
- Indocyanine green clearance
- Laser Doppler flowmetry
- Spectrophotometry
- Orthogonal polarizing spectral imaging
- Sidestream darkstream imaging
- Radiolabelled microspheres

Secondary Outcome: Mortality (death or self-defined surrogates of death)

Tertiary Outcomes: Hemodynamic parameters, fluid balance, acid-base status, cardiac biomarkers, kidney function, liver enzymes

All outcomes will be grouped by time of measurement: ≤ 6 h, 6-12 h, >12-≤24 h, and > 24 h following initiation of vasopressor

Data Extraction: Using DistillerSR®, two independent reviewers (TJ, ML) will extract data into pre-piloted forms

Risk of Bias Assessment: Cochrane Risk of Bias Assessment Tool³
- Random sequence generation
- Baseline characteristics
- Allocation concealment
- Blinding of personnel and outcome assessment
- Incomplete outcome data
- Selective outcome reporting

Construct Validity: Potential “clinical relevance” will be evaluated by
- Presence of intercurrent illness
- Use of an infectious model of sepsis
- Initiation of therapy after establishment of disease
- Use of concurrent therapy

Results

Study Flow

- 1605 retrieved during initial search
- 24 duplicates excluded
- 1781 reviewed by title screen
- 1087 unrelated topic excluded
- 674 reviewed by abstract screen* (This is an ongoing study)

Future Directions

- Abstract and Full Text screening will be completed
- Study Characteristic, Risk of Bias and Construct Validity data from the included studies will be extracted
- A priori defined outcome measures will be extracted

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References