VASOPRESSORS IN HEMORRHAGIC SHOCK

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CIRCULATORY SYSTEM

- Pump
  - Pumping force
  - Pumping rate
- Tank
  - Capacity
- Fluid
  - Volume
  - Nutrition & oxygenation capacity

Positive inotropic & chronotropic agents
Vasopressors
Volume expanders
PHYSIOLOGIC COMPENSATION
MECHANISMS FOR HEMORRHAGE

▪ Initial peripheral & mesenteric vasoconstriction to shunt blood to the central circulation
▪ Progressive tachycardia
▪ Increased CI, DO$_2$, & VO$_2$
A CLASSIC TRI-MODAL DISTRIBUTION OF DEATHS

1. Within minutes of hemorrhage due to immediate exsanguination

2. *After 1 to several hours due to progressive decompensation*

3. Days to weeks later due to sepsis & organ failure
PRE-HOSPITAL CONSIDERATIONS

**Rapid transport for definitive care**

- Stop bleeding
- Do not waste time for vascular access
- Consider permissive hypotension
STOP THE BLEEDING FIRST

Hemorrhage

Traumatic
- External
  - Non-controllable
  - Controllable
  - Femoral artery
  - Temporal artery
- Internal
  - Non-controllable
  - Intra-abdominal
  - Femoral or pelvic Fx.

Spontaneous
- External
  - Non-controllable
  - Rectorrhagia
- Internal
  - Controllable
  - Ant. epistaxis
  - Alveolar hemorrhage
  - Esophageal varice
DOES VASOPRESSOR THERAPY HAVE AN INDICATION IN HEMORRHAGIC SHOCK?

François Beloncle, Ferhat Meziani, Nicolas Lerolle, Peter Radermacher, & Pierre Asfar

Vasopressors & Bleeding

- A common practice among several pre-hospital & hospital emergency teams in Europe except in the UK
- No mention of vasopressor use in North American textbooks & European recommendations
  - No human studies exist to support
  - Their use early in the management of hemorrhagic shock may be harmful
Vasopressors & GI Bleeding

- IV vasopressin & H₂ blockers have been used.
  - Adverse reactions common
    - HTN
    - Arrhythmias
    - Gangrene
    - Myocardial or splanchnic ischemia
  - Should be considered secondary to more definitive measures
Microcirculatory effects of selective receptor blockade during hemorrhagic shock treatment with vasopressin: experimental study in the hamster dorsal chamber

In hemorrhagic shock, treatment with low-dose vasopressin, in combination with fluid therapy, improves tissue perfusion.
DATA SOURCE

- 15 experimental studies
- 3 retrospective clinical studies
- 1 controlled trial
- Published case reports were discarded.
Vasopressor support not appear to be indicated

Hemorrhage

Early phase

Sympathetic system activation

Compensatory venous & arterial vasoconstriction

Physiopathological arguments
Beyond a certain amount of blood loss

Sympathetic inhibition

A drop in vascular resistances & bradycardia

Cardio-circulatory arrest

Usefulness of rapid vasopressor injection to restore arterial BP & redirect CO toward vital organs?
OTHER FACTORS AFFECTING VASOCONSTRICTIVE RESPONSE

▪ Sedation & analgesia
▪ Shock duration
  ▪ Vasodilation in prolonged shock characterized by a deficiency of compensatory mechanisms
    ▪ An intense inflammatory response
    ▪ Global ischemia-reperfusion injuries resulting in up-regulation of cytokine expression & oxidative & nitrosative stresses
  ▪ A vascular hyporeactivity to norepinephrine mediated by an enhanced release of nitric oxide (NO), such as in septic shock
LONG-DURATION SHOCK EXPOSURE EXCEEDING SEVERAL HOURS

- Vasopressor support?
  - Extrapolating animal data to humans?

**Conditions?**
- **Vasopressor agent**
- **Timing of infusion?**
Additional Effects?

- Restoring hemodynamic parameters along with adequate vital organ infusion
  - Reducing the need for fluid
    - Side-effects, such as tissue (cerebral, pulmonary, etc.) edema
    - A systemic inflammatory response, in particular ARDS
      - The primary cause of death on Day 3 in trauma patients
Additional Effects?

- Abdominal lesions
  - Early vasopressor infusion
    - Splanchnic vasoconstriction (particularly pronounced following vasopressin use)
    - Decrease in portal output

*Decreased hemorrhagic loss from splanchnic blood vessels*  
*While maintaining adequate infusion of other organs*
Observations in Animal Models

- Associated cranial trauma
  - No effect on ICP
  - Effects of volume-sparing measures on pulmonary lesions & cerebral edema

*Need for initial fluid loading*
PROBLEMS OBSERVED IN ANIMAL MODELS

- Tissue hypoperfusion
  - Heart
  - Kidney
  - Gut (transient)
CLINICAL STUDIES

- 1 single, descriptive study reported
  - Dopamine use
  - In a general care protocol for polytrauma patients with life-threatening hemorrhage
  - From pelvic fractures
  - Associating early arteriography ± embolization
  - Along with vasopressor treatment initiated within the first hour of hospital admission
  - Better outcome
  - Not associated with any obvious detrimental effects

- Negative results in American studies
A prospective study assessed the effect of early vasopressin use in a double-blind, randomized trial.

- Control group (fluid alone, 40 patients)
- Treatment group (the addition of vasopressin, 4 IU bolus followed by 2.4 IU/h for 5 h, 38 patients)
- Lower fluid resuscitation volume over 5 days ($p = 0.04$) with a mortality rate at day 5 of 25% versus 13%, respectively ($p = 0.19$).
CONCLUSIONS

- Insufficient clinical evidence to validate early vasopressor use in association with fluid infusion in hemorrhagic shock management
- Type of vasopressor & the precise timing?
- The use of NE advocated by some teams appears reasonable (expert idea)
- Fluid loading is the first step to be considered in the management of hemorrhagic shock.
CLINICAL STUDIES WARRANTED

- A precise design in a setting in which definitive treatment is postponed

- European study conducted to assess the impact of vasopressin infusion as a salvage therapy in pre-hospital hemorrhagic shock that persists despite standard treatment, including a first line vasopressor (Vasopressin In Traumatic Shock (VITRIS) trial, NCT00379522), may provide an answer.
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