VASOPRESSORS IN HEMORRHAGIC SHOCK

Babak Mahshidfar, M.D.

Assistant Professor of Emergency Medicine

IUMS

Fellow of Iranian Society of Emergency Medicine (ISEM)

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

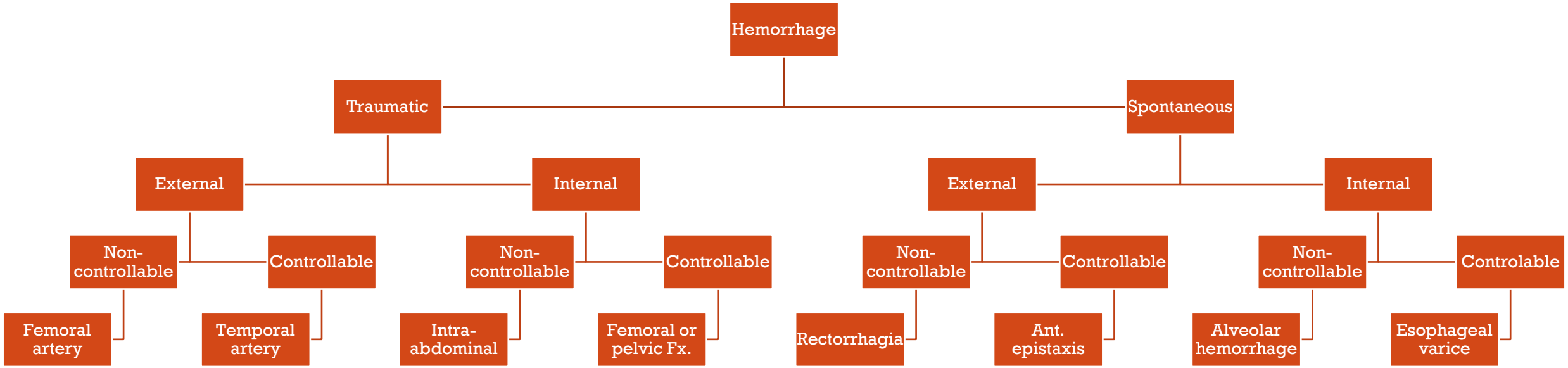
1. Within minutes of hemorrhage due to immediate exsanguination
2. ***After 1 to several hours due to progressive decompensation***
3. Days to weeks later due to sepsis & organ failure

PRE-HOSPITAL CONSIDERATIONS

Rapid transport for definitive care

- Stop bleeding
- Do not waste time for vascular access
- Consider permissive hypotension

STOP THE BLEEDING FIRST



DOES VASOPRESSOR THERAPY HAVE AN INDICATION IN HEMORRHAGIC SHOCK?

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

Ann Intensive Care. 2013; 3: 13

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 & H_2 blockers have been used.
  - Adverse reactions common
    - HTN
    - Arrhythmias
    - Gangrene
    - Myocardial or splanchnic ischemia
  - Should be considered secondary to more definitive measures

SHOCK 2012 NOV

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.

PHYSIOPATHOLOGICAL ARGUMENTS

Hemorrhage

Early phase

Sympathetic system activation

Compensatory venous & arterial vasoconstriction

Vasopressor support not appear to be indicated

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

CLINICAL 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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