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Clinical Investigation

CLINICAL INVESTIGATION

Effect of early use of noradrenaline on in-hospital mortality in haemorrhagic shock after major trauma: a propensity-score analysis

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This work has been presented at the annual conference of the French Society of Anaesthesiology and Critical Care in September 2016, and was awarded as the 'Best Abstract in Emergency Medicine'.

Abstract

Background: The role of vasopressors in trauma-related haemorrhagic shock (HS) remains a matter of debate. They are part of the most recent European recommendations on the management of HS and are regularly used in France. We assessed the effect of early administration of noradrenaline in 24 h mortality of trauma patients in HS, using a propensity-score analysis.

Methods: The study included patients from a multicentre prospective regional trauma registry. HS was defined as transfusion of ≥4 erythrocyte-concentrate units during the first 6 h. Patients with a Glasgow coma scale=3 and pre-hospital traumatic cardiac arrest were excluded. The main outcome measure was in-hospital mortality. The explicative and adjustment variables for the outcome and treatment allocation were predetermined by a Delphi method. The in-hospital mortality of patients with and without early administration of noradrenaline was compared in a propensity-score model, including all predetermined variables.

Results: Of 7141 patients in the registry in the study period, 6353 were screened and 518 patients in HS (201 with early noradrenaline use and 317 without) were included and analysed. After propensity-score matching, 100 patients remained in each group, and the hazard-ratio mortality was 0.95 (95% confidence interval: 0.45–2.01; P=0.69).

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Conclusions: The results of the present study suggest that noradrenaline use in the early phase of traumatic HS does not seem to affect mortality adversely. This observation supports a rationale for equipoise in favour of a prospective trial of the use of vasopressors in HS after trauma.

Keywords: noradrenaline; propensity score; shock; trauma

Editor's key points

- Data on the use of vasopressors in the management of haemorrhagic shock are conflicting and opinions are divided.
- This retrospective study of a large multicentre database analysed the effect of early administration of noradrenaline on outcome in trauma-related haemorrhagic shock.
- The propensity-score-matching analysis showed no effect of early noradrenaline use on in-hospital mortality.
- Randomised prospective data are required to confirm these findings.

The most recent update of the European recommendations on the management of haemorrhagic shock (HS) suggests the use of vasopressors, noradrenaline in particular, when fluid expansion fails to maintain the target arterial blood pressure.[1] However, the usefulness of vasopressors in the management of trauma-related HS remains a matter of debate.[2]

From a pathophysiological standpoint, opponents highlight increased oxygen consumption, increased cardiac afterload, and a potentially detrimental effect on regional perfusion[3,4] as arguments against vasopressor therapy. Proponents point out that vasopressors mimic the initial response to blood loss; improve venous return, coronary perfusion, and myocardial contractility[5]; and compensate for sedation-induced vasodilation and uncontrolled vasoplegia after exhaustion of physiological response mechanisms.[6]

Generally, vasopressors are considered to have a negative impact on patient outcome in the management of HS, and the predominant strategy is based on permissive hypotension and low-volume resuscitation.[7] We lack a high level of evidence studies on vasopressor use in HS in humans. Observational retrospective studies in humans indicate a higher mortality with the use of catecholamines in traumatic shock.[8–10]

More recent experimental and animal data suggest a beneficial influence of vasopressor use in association to a balanced low-volume resuscitation to restore perfusion[11,12] and preserve intestinal perfusion.[13,14] One small prospective randomised human trial indicates a survival benefit.[15]

This conflicting body of evidence justified exploring the association of noradrenaline administration with mortality in HS in trauma patients using a large multicentre observational registry. Our hypothesis was that early pre-hospital administration of noradrenaline in HS is not associated with an increased mortality. As treatment allocation was not controlled because of the observational nature of the data, we used propensity score (PS) to estimate the potential causal effect.

Methods

This is an observational study using a prospective multicentre trauma registry, the TraumaBase©. The TraumaBase obtained approval from the Institutional Review Board (Pr Laurent Capelle, Paris Cedex 13, France) (Comité de Protection des Personnes, Paris VI), from the Advisory Committee on Information Processing in Health Research (CCTIRS, 11.305bis), and from the National Commission on Informatics and Liberties (CNIL, 911461). The structure of the database integrates algorithms for consistency and coherence. A central administrator assures the data monitoring.

Between January 2010 and December 2015, all consecutive trauma patients triaged to one of the six regional, designated Level 1, trauma centres in Paris (Beaujon, Bicêtre, Pitié-Salpétrière, Henri-Mondor, Hôpital Européen Georges Pompidou, and Hôpital d'Instruction des Armées Percy) were screened for inclusion. A detailed description of the French Emergency Medical Services (EMS) and trauma system in Paris has been provided elsewhere.[16] At any time, clinical management was left to the discretion of the responsible physician (pre- or in-hospital) according to existing guidelines.[1] Pre- or intra-hospital vasopressor use in the Paris EMS system is almost exclusively equivalent to the continuous i.v. administration of noradrenaline. Noradrenaline was only to be used after a fluid challenge of around 1000–1500 ml of crystalloid (normal saline or Ringer's lactate, exceptionally colloids) had failed to restore the target arterial pressure according to the type of injury (blunt *vs* penetrating) according to a national guideline.[17] Pre-hospital use of noradrenaline was considered as the treatment regimen. Pre-hospital arterial pressure (systolic and diastolic) was recorded twice; the first measurement on the arrival of the enhanced care team on the scene, and then the lowest systolic and diastolic arterial-pressure readings, both before noradrenaline administration.

All trauma patients with HS were included. HS was defined in the registry as transfusion of more than four erythrocyte concentrates in the first 6 h of admission.[18,19] This definition of HS was chosen because transfusion requirements in the first 6 h seem better correlated with mortality than transfusion of at least three packed red blood cells (RBCs) in 1 h[20] or five packed RBC in 4 h.[21] Patients with a Glasgow coma scale (GCS) score of 3 or with pre-hospital cardiac arrest and younger than 16 yr were excluded.

Supplementary Table S1 provides the complete list of clinical, physiological [trauma mechanism, haemodynamic status, GCS, and peripheral oxygen saturation (SpO_2)], and biological variables (lactate, haemoglobin, and variation between pre- and in-hospital haemoglobin measurements) that were recorded for each patient. Calculation of the following scores completed this information: simplified acute physiology score II[22] and the sequential organ failure assessment[23] after 24 h. Trauma injury assessment was performed with the calculation of the injury severity score (ISS).[24]

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