Ray et al. Critical Care (2016) 20:293
DOI 10.1186/s13054-016-1473-4

Critical Care

LETTER Open Access

Real-life use of vasopressors and inotropes in cardiogenic shock—observation is necessarily 'theory-laden'

Samiran Ray[1,5*], Mirjana Cvetkovic[2], Daniel H. Lutman[1], Nazima Pathan[3], Padmanabhan Ramnarayan[1,4], David P. Inwald[4] and Mark J. Peters[1,5]

See related Research by Tarvasmäki et al., https://ccforum.biomedcentral.com/articles/10.1186/s13054-016-1387-1

We commend the attempt of Tarvasmäki et al. [1] to identify the mortality risk associated with individual vaso-active agents used in cardiogenic shock. However, despite their rigorous statistical analysis, we recommend caution in interpreting these results. Propensity score matching accounts for prior bias in the choice of vaso-active agents, but this choice of agent is often deeply engrained in individual clinician dogma which even propensity score matching may not uncover.

We recently conducted a similar retrospective analysis of vaso-active agents used in children with sepsis during stabilisation and transport of children by our paediatric intensive care transport service. Cold shock is common in sepsis in children, and the choice of vaso-active agent depends on the balance of inotropy or vasoconstriction needed. During transport, haemodynamic assessment is limited—choices of vaso-active agent used are made on limited data. Over a 7-year period (2005–2011), 364/633 (57.5 %) children were started at least on one vaso-active agent prior to intensive care unit admission. Epinephrine was associated with a crude mortality of 3.84 (95 % CI 2.5–5.91) compared to 1.8 (95 % CI 1.17–2.76) and 1.39 (95 % CI 0.91–2.1) for norepinephrine and dopamine, respectively. However, when standardised for risk using the PIM (Paediatric Index of Mortality) score, the standardised mortality ratio for epinephrine was 1.30 (95 % CI 0.98–1.63). When propensity score matching was used to account for choice of agent (calculated using age, weight, fluids administered, need for prior CPR, other agent use), no difference was seen between those who did and did not receive epinephrine (p value = 0.09). Yet Ventura et al. demonstrated, via a randomised controlled trial, that dopamine was associated with an increased mortality in children with sepsis compared to the use of epinephrine (OR 6.5, 95 % CI 1.1–37.8) [2]!

These contradictory findings are likely be a reflection of how different drugs are used—as the degree of statistical adjustment for confounding was improved (from crude to standardised mortality to propensity score matching), the initial mortality association with epinephrine use disappeared. When the use of drugs was protocolised in randomised controlled trial circumstances the association was reversed, with epinephrine showing a mortality benefit over dopamine. It is likely that more important than the choice of drug may be the use of the right amount of the right drug at the right time [3]. We join the authors to call for further randomised controlled trials to determine an evidence-based approach to vaso-active agent use.

* Correspondence: samiran.ray@gosh.nhs.uk
[1]Children's Acute Transport Service, Great Ormond Street Hospital NHS Trust, London WC1N 3JH, UK
[5]University College London Institute of Child Health, 30 Guildford Street, London, UK
Full list of author information is available at the end of the article

Additional file

Additional file 1: Contingency table with data used to calculate crude odd ratios of death for each vasoactive agent. (XLSX 11 kb)

Abbreviations
OR: Odds ratio; CI: Confidence interval

Acknowledgements
The authors would like to thank Ms Marissa Willock, Clinical Administrator, Children's Acute Transport Service, for her assistance with data collection.

Funding
This work was undertaken at Great Ormond Street Hospital/UCL Institute of Child Health, which received a proportion of funding from the Department of Health's NIHR Biomedical Research Centre's funding scheme.

Availability of data and materials
Contingency tables provided as Additional file 1.

Authors' contributions
The study was part of a wider project exploring the outcomes from sepsis in a transport service cohort. The study was conceived by MJP, PR, DI, DHL, and NP; data were collected by SR and MC; data were verified by SR and MJP; data were analysed by SR; the manuscript was written by SR, with review and comments from PR, DI, NP, MJP. All authors read and approved the final manuscript.

Authors' information
As title page.

Competing interests
The authors declare that they have no competing interests.

Ethics approval and consent to participate
The study was registered with the Institutional Audit Department (Project ref. 1014) as a wider service evaluation of the management of sepsis. It was discussed with the Bloomsbury Research Ethics Committee who waived a requirement for formal review.

Author details
[1]Children's Acute Transport Service, Great Ormond Street Hospital NHS Trust, London WC1N 3JH, UK. [2]University Hospitals of Leicester NHS Trusts, Leicester, UK. [3]Addenbrookes Hospital, Cambridge University Hospitals NHS Trust, Cambridge, UK. [4]Imperial College Healthcare NHS Trust, London, UK. [5]University College London Institute of Child Health, 30 Guildford Street, London, UK.

Published online: 26 September 2016

References
1. Tarvasmäki T, Lassus J, Varpula M, Sionis A, Sund R, Køber L, Spinar J, Parissis J, Banaszewski M, Silva Cardoso J, Carubelli V, Di Somma S, Mebazaa A, Harjola VP, CardShock study investigators. Current real-life use of vasopressors and inotropes in cardiogenic shock—adrenaline use is associated with excess organ injury and mortality. Crit Care. 2016; 20(1):208.
2. Ventura AM, Shieh HH, Bousso A, Góes PF, de Cássia FO, Fernandes I, de Souza DC, Paulo RL, Chagas F, Gilio AE. Double-blind prospective randomized controlled trial of dopamine versus epinephrine as first-line vasoactive drugs in pediatric septic shock. Crit Care Med. 2015;43(11):2292–302.
3. Rachoin JS, Dellinger RP. Timing of norepinephrine in septic patients: NOT too little too late. Crit Care. 2014;18(6):691.