Towards evidence-based emergency medicine: Best BETs from the Manchester Royal Infirmary

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BET 1: GIVE PREHOSPITAL BLOOD AND SAVE A LIFE?

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ABSTRACT

A short cut review was carried out to establish whether prehospital blood transfusion in the trauma patient with active haemorrhage can reduce mortality. 11 directly relevant papers were found using the reported search strategy. Of these two presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. It is concluded that prehospital blood transfusion may reduce short-term mortality in these patients, but that the evidence level is low and further definitive randomised controlled trials are needed to prove benefit.

CLINICAL SCENARIO

A 30-year-old male involved in a high-speed motorcycle accident is attended to by a prehospital critical care team. On scene the patient is moribund and in a shocked state. As the reversible causes of shock are addressed you wonder if resuscitation with blood products rather than crystalloid would improve the patient's chances of survival. Major haemorrhage protocols are used in hospital and intuition would suggest potential benefit if these protocols were administered at the point of injury, in order to reduce the later incidence of coagulopathy.

THREE-PART QUESTION

In [prehospital patients with traumatic haemorrhage] is [a blood transfusion superior to care without transfusion] at [reducing mortality]?

SEARCH STRATEGY

A literature search of EMBASE, MEDLINE and CINAHL was conducted via NHS Evidence. UK Blood Services Transfusion Evidence Library, Google Scholar were also searched.

Medline and CINAHL: [(prehospital*.ti.ab OR pre-hospital*.ti.ab OR "HEMS."ti.ab OR helicopter* adj2 emergenc*.ti.ab OR "air medic*".ti.ab OR "emergency medic* service*."ti.ab OR ground adj4 medic*) AND (exp WOUNDS AND INJURIES/OR h?emorrhag*.ti.ab OR trauma*.ti.ab) AND (exp BLOOD TRANSFUSION/OR "red blood cell*."ti.ab OR plasma adj2* transfuse*.ti.ab OR fresh frozen plasma."ti.ab)] [LIMIT to English and Human].

EMBASE (date of searching 2 March): [(prehospital*.ti.ab OR pre-hospital*.ti.ab OR "HEMS."ti.ab OR helicopter* adj2 emergenc*.ti.ab OR "air medic*".ti.ab OR "emergency medic* service*."ti.ab OR ground adj4 medic*) AND (exp INJURY/OR h?emorrhag*.ti.ab OR trauma*.ti.ab) AND (exp BLOOD TRANSFUSION/OR "red blood cell*."ti.ab OR plasma adj2* transfuse*.ti.ab OR fresh frozen plasma."ti.ab)] [LIMIT to English and Human].

EMBASE; 265 papers, MEDLINE; 104 papers, CINAHL; 57 papers, UK Blood Services Transfusion Evidence Library; 121 papers, Google Scholar; 50 papers.

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MeSH descriptor: [Blood Transfusion] explode all trees AND prehospital ti, ab. kw=4 results

OUTCOME

After review of title and abstract 11 papers were found and reviewed in full. Seven were excluded after full text review due to the following: three poor quality, two wrong comparison group, one descriptive study and one unpublished study (table 1).

COMMENTS

All of the studies included are of a retrospective observational design and are therefore subject to selection bias and confounding. In addition, several are distinct 'before and after' comparisons, a methodology which has numerous flaws and limited ability to assess causation (Goodacre *et al* 2015).[5] The dependence on evidence from observational studies is common in the setting of prehospital trauma care; the number of high-quality randomised control trials is small and design is challenging across regions with variable geography, medical response

Table 1 Relevant papers

Author, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
O'Reilly *et al*, 2014,[1] UK	1592 casualties over a 6-year period. Introduction of prehospital blood transfusion (PHBTX) by MERT-E in 2008 created two cohorts ie, a pre-PHBTX and post-PHBTX era. 97 patients were matched. 26.9% received a PHBTX of PRBC and FFP.	Retrospective matched cohort study	Mortality (no PHBTX vs PHBTX)	19.6% vs 8.2% (p<0.001)	Losses to follow-up. Multiple potential confounders were identified: recipients of a PHBTX received more prehospital interventions (eg, chest decompression, advanced airway intervention, tranexamic acid, larger total blood infusions, improved ratios of PRBC: FFP and shorter prehospital times). No statistical analysis was used to control for these confounders.
Holcomb *et al*, 2015,[2] USA	885 prehospital trauma patients transported by two different HEMS (LF and OA) operations. Comparison was made between cohorts of 716 patients with LF with available blood products and 169 patients with OA resuscitated with crystalloid only. 19% of the LF received a PHBTX of PRBC and FFP.	Retrospective cohort study	Mortality at 6 h among those with critical ED disposition (admitted directly to the ICU, IR, OR or morgue) Mortality at 24 h Mortality at 30 days	OR 0.23 (95% CI 0.0062 to 0.890; p=0.033) OR 0.57 (p=0.117) OR 0.71 (p=0.441)	Differences in critical care capabilities between the HEMS were not discussed in detail. Ground platforms are excluded from analysis due to 'gross inequities' and represent selection bias. No matching of patients was attempted in this study. LF shared its governance with the major trauma centre, possibly representing a conflict of interests. No breakdown in injury type. Marked differences in transport times.
Brown *et al*, 2015,[3] USA	8616 prehospital trauma patients transport by air to a level 1 trauma centre. Matched cohort of 213 was created. 2.9% received a PHBTX of PRBC.	Retrospective matched cohort study	Survival at 24 h Survival in hospital	AOR 6.32 (95% CI 1.88 to 21.14; p <0.01) AOR 4.32 (95% CI 0.76 to 24.72; p=0.10)	Single-centre study using a single HEMS operation. Potential for selection bias. Missing data. Initial large crystalloid infusions. Survival bias. PRBC transfusion only.
Brown *et al*, 2015,[4] USA	1415 civilian patients with blunt trauma transferred to a trauma centre. A matched cohort of 113 was created. 3.5% received a PHBTX of PRBC ±plasma.	Retrospective cohort study	Mortality at 24 h Mortality at 30 days	AOR 0.02 (95% CI 0.01 to 0.69; p=0.04) AOR 0.12 (95% CI 0.03 to 0.61; p=0.01)	Small numbers of transfusions. 2 h cut-off creating selection bias. Missing data. No description of the capabilities of the prehospital provider. No data regarding type of transfusions or ratios of blood products. Survival bias. Blunt trauma only.

MERT-E, medical emergency response team; FFP, fresh frozen plasma; HEMS, helicopter emergency medical service; LF, life flight; OA, other agencies; ICU, intesive care unit; AOR, adjusted odds ratio; PRBC, packed red blood cells.

times, patient demographics and levels of medical response. In conclusion, all of the four papers suggest an early survival benefit (6–24 h), however there is limited evidence of a sustained reduction in mortality. These data are also level 4 evidence only and conclusions should therefore be regarded as hypothesis generating. The feasibility of delivering prehospital blood has been demonstrated in multiple cohort studies (Rehn *et al* 2015).[6] It is the effectiveness, cost, resource implications and risk/benefit profile that remain in question. Several future studies are planned that may help address these questions (Reynolds *et al* 2015, Dretzke *et al* 2014, RePHIL).[7–9]

Clinical bottom line

There is a potential clinical benefit in prehospital blood transfusion. However, this has not been confirmed with high-level evidence and potential harms/costs remain unquantified. Further high-quality randomised control trials are needed, with stratified design accounting for injury type, scene times and prehospital response.

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