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SHORT REPORT

Blood culture collection and administration of intravenous ceftriaxone by paramedics in patients with suspected sepsis (the pass trial)

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Abstract

Objective: To evaluate the feasibility of pre-hospital blood culture (BC) collection and intravenous (IV) antibiotic administration in patients with suspected sepsis.

Methods: In this open-label trial, BCs were collected in all participants, who were then randomised to ongoing care (control) or ongoing care plus 2 g IV ceftriaxone (intervention). Time to antibiotic administration was the primary outcome.

Results: Thirty-five patients were enrolled and randomised (21 control, 14 intervention). BCs were obtained in 89% ($n = 31/35$) and grew a pathogen in 42% ($n = 13/31$). Intervention patients received antibiotics a median of 108 (95% CI 34 to 170) minutes earlier ($P < 0.01$).

Conclusion: BCs were successfully obtained by paramedics, and pre-hospital IV ceftriaxone resulted in expedited antibiotic administration.

Clinical Trial Registration: ACTRN12618000199213.

Key words: *antibotics, blood culture, ceftriaxone, EMS, out of hospital, paramedic, pre hospital, sepsis.*

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Introduction

Sepsis is a critical health issue in Australia,[1] with patients requiring ambulance transport manifesting particularly poor outcomes.[2] International guidelines recommend prompt blood culture (BC) collection and early intravenous (IV) antibiotic administration.[3,4] Currently, there are no Australian data on whether pre-hospital antibiotic administration results in improved time to therapy or if BCs can be successfully obtained by paramedics. As such, we conducted a randomised clinical trial to assess the feasibility of delivering such care in this setting.

Methods

Study design and patient population

This was a prospective, randomised open-label trial conducted between

TABLE 1. *Patient characteristics and outcomes*

	Intervention ($n = 14$)	Control ($n = 21$)
Patient characteristics		
Age, median [IQR]	70 [60–77]	81 [72–87]
Male sex, *n* (%)	10 (71.4)	13 (61.9)
Comorbidities, *n* (%)		
Respiratory	9 (64.3)	6 (28.6)
Cardiovascular	9 (64.3)	14 (66.7)
Hepatic	1 (7.1)	0 (0)
Immunosuppressive therapy	5 (35.7)	4 (19.0)
Dialysis dependent	0 (0)	2 (9.5)
Vital signs, median [IQR]		
SBP (mmHg)	84 [79–89]	81 [71–93]
RR (/min)	30 [23–39]	26 [20–34]
GCS	13 [13–14]	14 [13–14]
Body temperature (°C)	37.7 [36.1–39.0]	38.1 [37.2–39.2]†
NEWS2 Score, median [IQR]	13 [10–14.3]	13 [10–14.5]
Pre-hospital care		
Region of enrolment		
Metropolitan, *n* (%)	2 (14.3)	6 (28.6)
Rural, *n* (%)	12 (85.7)	15 (71.4)
Scene time, minutes, median [IQR]	37 [25–49]	43 [37–54]
Transport time, minutes, median [IQR]	48.5 [30–64]	34 [23–71]
Pre-hospital BC obtained, *n* (%)	10 (71.4)	21 (100)
Pre-hospital IV ceftriaxone, *n* (%)	12 (85.7)‡	1 (4.8)§
Emergency department assessment		
White cell count, $\times 10^9$/L, median [IQR]	13.2 [8.2–16.3]	12.4 [8.8–20.4]
Lactate, mmol/L, median [IQR]	3.0 [1.7–6.5]	2.2 [1.3–5.1]†
Vasoactive, *n* (%)	9 (64.3)	10 (47.6)
Mechanical ventilation, *n* (%)	5 (35.7)	2 (10)¶
Need for ICU admission, *n* (%)	6 (42.9)	9 (42.9)
Pathogen grown in pre-hospital BC, *n* (%)	6 (42.9)	7 (33.3)
In-hospital characteristics		
Hospital length of stay, days, median [IQR]	5.4 [2.2–7.5]	4.3 [2.5–8.3]¶
In-hospital mortality, *n* (%)	4 (28.6)	6 (28.6)

†Data not available for two patients. ‡One patient reported a cephalosporin allergy after enrolment, and continued IV access was not possible in another. §IV ceftriaxone administered enroute by receiving hospital. ¶Data not available for one patient. BC, blood culture; C, Celsius; GCS, Glasgow Coma Score; ICU, intensive care unit; IQR, interquartile range; IV, intravenous; NEWS2, National Early Warning Score 2; RR, respiratory rate; SBP, systolic blood pressure.

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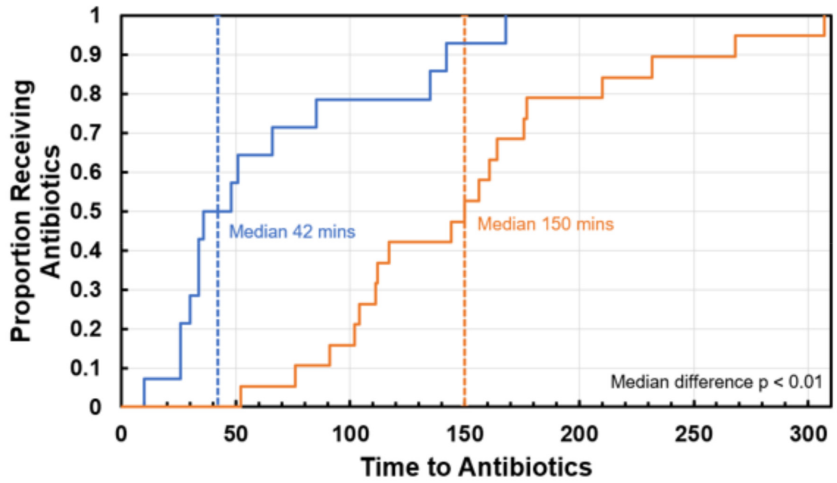

Figure 1. *Time to antibiotics. Time to antibiotics was calculated as the difference between paramedic arrival on scene and administration of first recorded antibiotics pre-hospital or in hospital. This includes the two patients where the first dose was in hospital in the intervention group and the one patient in the control group who received IV ceftriaxone during transport.*

01 March 2018 and 01 August 2023. Patients were eligible if they were ≥18 years of age, were being transported to a participating hospital, and met the following criteria: history suggestive of infection, systolic blood pressure < 100 mmHg, and Glasgow Coma Score < 15.[5] See Supporting Information for additional exclusion criteria.

Enrolment, randomisation and data collection

All patients had a peripheral IV cannula inserted, and two sets of BCs obtained. Patients were then randomised 1:1 to either standard care (control) or standard care plus 2 g IV ceftriaxone (intervention), and transported to hospital. Data were extracted from pre-hospital and hospital patient care records. Skin commensals, not grown in subsequent BCs, were considered contaminants.

Study outcome

Time from arrival at the scene to first antibiotic administration was the primary outcome. Exploratory variables included BC results, scene & transport times, need for ICU, hospital length of stay, and in-hospital mortality. Pre-specified adverse events were also recorded.

Statistical analysis

Categorical variables are expressed as counts (%), continuous variables as median [IQR]. Time to antibiotic administration was analysed using the log-rank test and quantile regression, reported as the median difference, 95% confidence interval (CI). A two-sided P value of 0.05 was considered significant. The study planned to enrol 110 patients (55 in each arm), with >95% power to detect a 60-min difference in time to antibiotic administration.

Ethics and consent

Ethical approval (with waiver of individual patient consent) was provided by The Alfred Health Human Research Ethics Committee (HREC/18/Alfred/26). Participants/surrogates could opt out of data collection.

Results

Study patients

Thirty-five patients were enrolled and randomised; 21 to the control group and 14 to the intervention group (see Supporting Information). The study was repeatedly paused because of COVID-19 and stopped prematurely in August 2023. Patient characteristics and outcomes are summarised in Table 1.

Pre-hospital BC collection and antibiotic administration

Blood cultures were obtained in 89% ($n = 31/35$) of participants. Two intervention patients did not receive IV ceftriaxone, while one control patient did (enroute). Antibiotics were administered a median of 42 min (IQR 31–85) after paramedic arrival in the intervention group, and 150 min (IQR 108–177, $P < 0.01$) in the control group; median difference 108 min, 95% CI 34 to 170 min (see Fig. 1).

Microbiological data

Thirteen of 31 (42%) BCs isolated bacterial pathogens, and four (4/31; 13%) grew contaminants (see Supporting Information). Three ($n = 3$) organisms were resistant to ceftriaxone.

In-hospital assessment

Sepsis was confirmed in 64.3% (9/14) of the intervention group and 80% (16/20) of the control group. All intervention patients received IV antibiotics in hospital, as did 90.5% ($n = 19/21$) of the control group. Additional exploratory variables are presented in Table 1. No pre-defined adverse events were reported.

Discussion

Approximately 90% of study participants had BCs drawn successfully, with over 40% isolating a bacterial pathogen. Patients were enrolled in both a regional and metropolitan setting. Moreover, administration of 2 g IV ceftriaxone pre-hospital reduced time to antibiotic therapy by a median of 108 (95% CI 34–170) minutes. Some patients were ultimately not considered septic, reflecting the inherent challenges of pre-hospital medicine. As such, a 'blanket' policy of antibiotic administration is clearly not

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appropriate; however, pre-hospital BC collection and IV antibiotic administration were both feasible and safe.

While supportive of future research in this area, our results are entirely preliminary and very much inconclusive. Indeed, with an open-label design resulting in likely treatment bias, a number of unmeasured confounders will have influenced the results. Finally, with a much smaller sample size than anticipated and considering the inherent heterogeneity of sepsis, the trial is grossly under-powered. This has also led to important differences in baseline characteristics between the two groups, likely because of chance.

Conclusion

In this preliminary study of patients with suspected sepsis, pre-hospital BCs could be successfully obtained in the majority, and in those randomised to IV ceftriaxone, antibiotic therapy was administered earlier. Future clinical trials assessing the clinical impact of this should be considered, with further refinement of patient selection.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's web site:

Data S1: Supporting Information.

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