Blood cultures in acute surgical admissions

DFJ Dunne, R McDonald, R Ratnayake, HZ Malik, R Ward, GJ Poston, SW Fenwick

Aintree University Hospital NHS Foundation Trust, UK

ABSTRACT

INTRODUCTION Obtaining blood cultures prior to the administration of antimicrobial therapy was a key recommendation of the 2012 UK Surviving Sepsis Campaign. Few studies have examined the effect blood cultures have on clinical management and there have been none on acute surgical admissions. This retrospective study sought to evaluate the effect of blood cultures on clinical management in acute surgical admissions.

METHODS Data on acute surgical patients admitted between 1 January and 31 December 2012 were extracted from hospital records. Patients given intravenous antibiotics within 24 hours of admission were identified. Data collected included antibiotics administered, blood culture results, admission observations and white blood cell count. Case notes were reviewed for patients with positive cultures to establish whether the result led to a change in management.

RESULTS Of 5,887 acute surgical admissions, 1,346 received intravenous antibiotics within 24 hours and 978 sets of blood cultures were taken in 690 patients. The recommended two sets of cultures were obtained in 246 patients (18%). Patients who had blood cultures taken had the same in-hospital mortality as those who had none taken (3.6% vs 3.5%, $p=0.97$). Blood cultures were positive in 80 cases (11.6%). The presence of systemic inflammatory response syndrome did not increase positivity rates (12.9% vs 10.3%, $p=0.28$). Overall, cultures altered management in two patients (0.3%).

CONCLUSIONS Blood cultures rarely affect clinical management. In order to assess the additional value that blood cultures bring to sepsis management in acute surgical admissions, a prospective randomised trial focusing on outcome is needed.

KEYWORDS

Sepsis – Emergency surgery – Blood cultures – Surviving Sepsis

Accepted 29 August 2014

CORRESPONDENCE TO

Declan Dunne, E: ddunne@nhs.net

Obtaining blood cultures prior to the administration of antimicrobial therapy was a recommendation of the 2012 UK Surviving Sepsis Campaign.¹ Blood cultures are purported to improve outcomes by ensuring appropriate antibiotic therapy in patients with sepsis.² They have been shown to detect 80% of patients with bacteraemia when one set of cultures is taken, rising to over 90% when two sets of cultures are taken prior to antimicrobial therapy administration.³ In medical patients with evidence of systemic inflammatory response syndrome (SIRS), blood cultures have been shown to be positive in 24% of cases, as opposed to 14% of those without SIRS.⁴

Best practice is now considered as performing two sets of cultures from separate sites, prior to antimicrobial treatment, in patients with suspected sepsis and evidence of a systemic inflammatory response. Inappropriate antibiotic treatment will do little to treat the infection and is associated with the development of *Clostridium difficile* infection, which is increasingly prevalent and a significant cause of morbidity.⁵

Despite the seemingly sensible rationale, questions have been raised regarding the benefit that blood cultures bring to sepsis management and how to best target their use.⁶ The overall rate of positivity of blood cultures is low, with

rates varying from 6.6% to 15%, falling to 4.1–7% when contaminants are excluded.^{7,8} Contaminants have been reported to result in false positive blood cultures in anywhere between 2.4% and 50% of cases.^{7–11} These false positive results have been associated with prolonged hospitalisation and a 20% increase in healthcare cost.¹² Blood cultures have been shown to have little effect on clinical management in women with pyelonephritis and acutely unwell surgical patients.^{13,14} Even the 2012 Surviving Sepsis Campaign acknowledged this weakness when it classified its recommendation as 1C (highly recommended but low evidence base).¹

The economic impact of implementing the Surviving Sepsis Campaign management guidelines in a UK National Health Service (NHS) setting has not been evaluated. However, in a US setting, blood cultures (and in particular false positive results) were associated with a significant healthcare cost.^{12,15–17} Given the uncertainty surrounding the additional benefit that blood cultures bring to sepsis management and the increasing financial pressures on the NHS, it is important to reassess the additional value that blood cultures bring to sepsis management. This retrospective study sought to evaluate the effect of blood cultures on clinical management in acute surgical admissions.

Methods

The study was approved by the local audit department. All patients admitted as an emergency to the surgery department at Aintree University Hospital between 1 January and 31 December 2012 were identified from computerised hospital records. This included all patients with an unscheduled admission to general surgery, hepatobiliary surgery, colorectal surgery, upper gastrointestinal surgery and urology. Using computerised pharmacy records, all patients who had intravenous (IV) antibiotics administered within 24 hours of admission time were identified. IV antibiotic administration was used as a surrogate marker for 'clinical impression of infection' as per the Surviving Sepsis Campaign guidelines. All clinical case notes during the study period were electronic and therefore retrievable. Mortality was defined as any in-hospital death.

Defining SIRS

All case notes were reviewed so as to extract admission observations. Laboratory records were interrogated to record the admission white blood cell count and C-reactive protein levels. A systemic inflammatory response was defined as the presence of two or more of:

- > temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$
- > heart rate >90 beats per minute
- > respiratory rate >20 breaths per minute
- > white blood cell count $<4 \times 10^9/\text{l}$ or $>12 \times 10^9/\text{l}$

Blood cultures

The clinical laboratory records were used to identify those patients who had blood cultures performed and the total number of sets of blood cultures performed. Unfortunately, as blood cultures were recorded electronically, it was only possible to establish the date of collection rather than the specific time. This was partly behind the decision to use admission observations to define the presence of sepsis and SIRS. Owing to difficulties in establishing the exact timing of cultures and to prevent excluding cases inappropriately, blood cultures obtained within 48 hours of admission were included in the study. Blood culture results were collated with the sensitivities of identified organisms. A blood culture was considered positive if any organism

was identified. For patients in whom more than one set of bloods cultures were performed, all results were amalgamated and defined as positive if one set of cultures identified at least one organism.

Defining effect on clinical care

All antibiotic therapy given during the course of each patient's admission was recorded. Establishing the effect of blood cultures on clinical care was limited by case note quality and an 'effect' was therefore defined as a change of antibiotic prescribing. A full case note review was undertaken if a blood culture was positive and the antibiotics delivered were outside of trust policy or if the organism identified was resistant to the antibiotics prescribed.

Blood culture collection

Blood cultures were collected using the BACTEC™ (BD, Oxford, UK) instrumented blood culture system. Local hospital policy directs that appropriately trained personnel must collect all blood cultures using full aseptic technique. Owing to the retrospective nature of this study, it was not possible to confirm that this policy was adhered to in all cases. The blood was cultured under standard laboratory conditions. Any organisms identified were relayed to the clinical team.

Antibiotic policy

Our local antibiotic policy is summarised in Table 1. For the majority of patients, piperacillin/tazobactam was the first-line treatment, with cefalexin and metronidazole being the oral step-down choice. In patients with penicillin allergy, the first-line choice was vancomycin with gentamicin and metronidazole, with oral step-down antibiotics based on advice from a microbiologist. There were no set policies on length of antibiotic therapy in patients with or without positive cultures.

Statistical analysis

Continuous normal data were analysed using a t-test and the Mann-Whitney U test was used for continuous data with a non-normal distribution. Categorical data were analysed using a chi-squared test. All statistical tests were conducted with SPSS® version 20.0 (IBM, New York, US).

Table 1 Local antibiotic guidelines

Suspected source of sepsis	First-line antibiotics	Penicillin allergy
Gastrointestinal	IV piperacillin/tazobactam; oral step-down regime: cefalexin and metronidazole	IV vancomycin, IV gentamicin and IV metronidazole; oral step-down regime: based on microbiological advice
Biliary	IV piperacillin/tazobactam; oral step-down regime: cefalexin and metronidazole	IV vancomycin, IV gentamicin and IV metronidazole; oral step-down regime: based on microbiological advice
Complicated/upper urinary tract infection	IV piperacillin/tazobactam	IV gentamicin; oral step-down regime: based on microbiological advice
IV = intravenous		

Results

There were 5,887 acute surgical admissions during the study period. The demographics of the study cohort are summarised in Table 2. There were significant differences in the demographics of the cohort receiving antibiotics within 24 hours of admission. Of all acute surgical admissions, 1,346 patients had IV antibiotics administered within 24 hours. This cohort was significantly older (median age: 56 vs 50 years), had a greater proportion of female patients (56% vs 52%) and longer admissions (median: 4 vs 2 days, $p<0.001$). Patients receiving IV antibiotics within 24 hours of admission were also significantly different from the overall cohort of emergency admissions in terms of method of admission, specialty of admission and method of discharge. As expected, mortality was also significantly higher in the group receiving IV antibiotics (3.5% vs 1.5%, $p<0.001$).

Adherence to surviving sepsis guidance

Of the 1,346 patients receiving IV antibiotics, only 690 had blood cultures performed. In total, 978 sets of blood cultures were collected and 246 patients had the minimum

recommended two sets of blood cultures performed, giving an overall adherence to the 2012 Surviving Sepsis Campaign of just 18%.

SIRS and blood culture collection

SIRS was present on admission in 600 of the 1,346 patients. Of the 600 patients, 332 had blood cultures performed. This meant that 268 patients (44.7%) with confirmed SIRS receiving IV antibiotic therapy within 24 hours did not have the cultures performed. The presence of SIRS increased the likelihood of blood cultures being collected (55% SIRS vs 48% no SIRS, $p=0.01$). Evidence of SIRS was also associated with a non-significant trend towards having multiple sets of cultures performed (SIRS 130/332 [39%] vs no SIRS 116/358 [32%], $p=0.07$).

Blood culture positivity

Of the 690 patients who had blood cultures performed, only 80 (11.6%) had an organism identified. There was no significant difference in blood culture positivity in those with SIRS (43/332) and without (37/358) ($p=0.28$). Patients who had more than one set of cultures performed were

Table 2 Demographics of surgical admissions

	Overall	Receiving IV ABs within 24 hours	p-value
Total admissions	5,887	1,346	–
Median age on admission (years)	50 (IQR: 32–68)	56 (38–72)	<0.001
Median length of stay (days)	2 (IQR: 0–4)	5 (3–9)	<0.001
Sex			<0.001
Male	2,828 (48%)	595 (44%)	
Female	3,059 (52%)	751 (56%)	
Method of admission			<0.001
A&E	4,211 (71.5%)	966 (71.2%)	
GP referral	1,416 (24.0%)	307 (22.8%)	
Outpatient clinic	57 (1.0%)	48 (3.6%)	
In-hospital transfer	25 (0.4%)	11 (0.8%)	
Other	178 (3.0%)	14 (1.0%)	
Specialty of admission			0.002
General surgery	3,909 (66.4%)	869 (64.6%)	
Colorectal surgery	644 (10.9%)	170 (12.6%)	
Hepatobiliary surgery	442 (7.5%)	122 (9.1%)	
Upper GI surgery	290 (4.9%)	83 (6.2%)	
Urology	602 (10.2%)	102 (7.6%)	
Method of discharge			<0.001
Died during admission	86 (1.5%)	48 (3.6%)	
Self-discharged	148 (2.5%)	11 (0.8%)	
Discharged on medical advice	5,653 (96.0%)	1,287 (95.6%)	
IV ABs = intravenous antibiotics; IQR = interquartile range; A&E = accident and emergency; GP = general practitioner; GI = gastrointestinal			

Table 3 Blood cultures in relation to systemic inflammatory response

	Total number of patients	Systemic inflammatory response		p-value
		Yes	No	
Received antibiotics within 24 hours	1,346 (100%)	600 (44.6%)	746 (55.4%)	N/A
At least one set of cultures performed				0.01
Yes	690 (51.3%)	332 (55.3%)	358 (48.0%)	
No	656 (48.7%)	268 (44.7%)	388 (52.0%)	
Two or more sets of cultures performed				0.07
Yes	246 (35.7%)	130 (39.1%)	116 (32.4%)	
No	444 (64.3%)	202 (60.8%)	242 (67.6%)	
Patients with a positive culture	80 (11.6%)	43 (12.9%)	37 (10.3%)	0.28
Patients with a resistant organism identified	8 (1.2%)	3 (0.9%)	5 (1.4%)	0.79
Patients where management was changed	2 (0.3%)	0 (0%)	2 (0.6%)	0.50
In-hospital mortality				
Overall	48 (3.6%)	23 (3.8%)	25 (3.4%)	0.66
Cultures	25 (3.6%)	12 (3.6%)	13 (3.6%)	0.97
No cultures	23 (3.5%)	11 (4.1%)	12 (3.1%)	

more likely to have a positive culture (37/246 [15.0%] vs 43/444 [9.7%], $p<0.05$).

Antibiotic resistance and effect on clinical management

In 8 of the 80 cases with positive blood cultures, the organisms identified were resistant to the prescribed antibiotics. Resistant organisms included four cases of *Escherichia coli*, one coagulase negative *Staphylococcus*, one *Klebsiella pneumoniae*, one *Streptococcus parasanguinis* and one *Aggregatibacter aphrophilus*. One of the eight patients died within twenty-four hours of admission, prior to the blood culture result being available.

Following microbiology and clinical review, three of the resistant organisms were considered contaminants (one coagulase negative *Staphylococcus*, one *Streptococcus parasanguinis* and one *Klebsiella pneumoniae*) and ignored. This left four cases where clinical management could have been altered as a result of the culture findings.

Of these, two patients with urinary retention and urinary tract infection were clinically improved at the time of the blood culture result becoming available and the result was consequently dismissed. The remaining two patients where clinical management was altered did not have any evidence of a systemic inflammatory response during their admission. The first was admitted with an abdominal collection following liver surgery and was well throughout admission; this patient underwent percutaneous drainage and antibiotics were swapped from piperacillin/tazobactam to meropenem as a consequence of the blood culture result. The second patient was admitted with mild cholangitis and at the time of the blood culture result, had already undergone endoscopic retrograde cholangiopancreatography. The blood culture result altered the step-down oral antibiotic choice from cefalexin to ciprofloxacin. Overall,

blood cultures altered clinical management in just 2 (0.3%) of the 690 patients cultured.

Discussion

This study has demonstrated that performing blood cultures in acute surgical admissions rarely affects clinical management. This is likely to be a result of a combination of factors including the low positive rate of cultures, the low incidence of detected resistant organisms and the success of the local antimicrobial policy. While adherence to the Surviving Sepsis Campaign recommendations on blood cultures was low, the results would question the value of attempting to meet its recommendation of obtaining blood cultures in all patients.

The presence or absence of SIRS had little effect on blood culture positivity or on overall in-hospital mortality. This is in contrast to previous suggestions that SIRS is a good discriminator in identifying patients where blood cultures are likely to be positive.^{6,7} The rate of blood culture positivity was significantly lower than the 24% found in medical admissions with SIRS,⁷ suggesting that in acute surgical admissions, the likelihood of detecting bacteraemia is lower. The rate of blood culture positivity in our study is more in line with previously reported findings of positive blood culture results of 6.6–15%.^{7,8} The absence of a significant difference in the rate of in-hospital mortality between cohorts (SIRS vs non-SIRS) indicates that SIRS criteria may not be as useful in identifying patients at increased risk of mortality in this population.

Performing two sets of cultures appeared to lead to a higher rate of blood culture positivity. Unfortunately, owing to the study design, the results of this study cannot be used to justify the Surviving Sepsis Campaign recommendation

to perform two sets of cultures.^{1,5} Local policy during the study period recommended performing additional blood cultures in patients with persisting signs of sepsis (ie those with SIRS criteria). As a result of difficulties in timing the collection of cultures, this study included cultures taken within the first 48 hours of admission. Some patients with persistent evidence of sepsis will therefore have been included in the 'two sets of cultures' group. Consequently, the increased positivity in the group where two or more sets of blood cultures were taken may reflect patients with more severe sepsis rather than an increased rate of positivity when two sets of cultures are taken.

Adherence to Surviving Sepsis Campaign recommendations on blood cultures was poor. However, the results of this study do not seem to support increasing emphasis on blood culture collection in all acute admissions given that there was no difference in the in-hospital mortality between patients with and without blood cultures performed. Despite the recommendations to deliver antibiotics without delay in patients with sepsis, performing blood cultures in an acute setting takes time and could lead to delays in antibiotic administration. Increasing blood culture collection will also inevitably lead to a rise in false positive results, with an associated prolonged length of stay and increased healthcare costs.¹⁷

This is a retrospective study of practice, rather than a prospective randomised controlled trial. A certain degree of caution is therefore needed when interpreting the results. One particular weakness of the study was that it was not possible to establish the exact time of blood culture collection with respect to antibiotic administration. While current hospital policy suggests collection of cultures prior to antimicrobial therapy, this cannot be verified. This could mean that the rate of positive cultures was depressed by sets of cultures taken following antimicrobial therapy administration. It is also important to note that the study did not look at the effect of culturing the primary site of sepsis but only at that of blood cultures. As such, it can offer no assessment of the value of culturing the suspected source of sepsis.

It would have been useful to establish a cohort of patients where two independent sets of cultures were taken prior to antimicrobial therapy. This would have enabled rates of positivity and effect on management to be established where Surviving Sepsis Campaign recommendations on blood cultures were followed. This is an area that would benefit from future study.

Our study assessed the effect of blood cultures on changes in antibiotic prescribing, not on patient outcome. This prescribing effect was limited by the quality of case notes to a change of antibiotics, rather than its effect on length and route of antibiotic delivery. This will serve to underestimate the role of blood cultures in this context. Ideally, to assess the role of blood cultures, a prospective randomised trial assessing mortality, morbidity and economic burden is needed. Furthermore, we did not address the role blood cultures play in defining local antibiotic policy, which appeared highly effective in this study as it covered 90% of identified pathogens.

Conclusions

The findings of this study suggest that blood cultures rarely alter the clinical management of acute surgical admissions and do not support the widespread adoption of the Surviving Sepsis Campaign guidelines on blood cultures in all acute surgical admissions with evidence of sepsis. In order to establish the additional value that blood cultures bring to sepsis management in acute surgical admissions, a prospective randomised trial focusing on outcome is urgently needed.

Acknowledgements

We would like to thank Dr Richard Cooke, Consultant Microbiologist, for his help in preparing the manuscript.

The material in this paper was presented at the 17th Annual Scientific Meeting of the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland held in Newcastle, September 2013.

References

1. Dellinger RP, Levy MM, Rhodes A *et al*. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med* 2013; **39**: 165–228.
2. Lee CC, Hong MY, Chan TY *et al*. The impact of appropriateness of antimicrobial therapy in adults with occult bacteraemia. *Emerg Med J* 2014; **31**: 53–58.
3. Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of bloodstream infections in adults: how many blood cultures are needed? *J Clin Microbiol* 2007; **45**: 3,546–3,548.
4. Jones GR, Lowes JA. The systemic inflammatory response syndrome as a predictor of bacteraemia and outcome from sepsis. *QJM* 1996; **89**: 515–522.
5. Morris AM, Jobe BA, Stoney M *et al*. *Clostridium difficile* colitis. *Arch Surg* 2002; **137**: 1,096–1,100.
6. Coburn B, Morris AM, Tomlinson G, Detsky AS. Does this adult patient with suspected bacteremia require blood cultures? *JAMA* 2012; **308**: 502–511.
7. Bates DW, Cook EF, Goldman L, Lee TH. Predicting bacteremia in hospitalized patients. A prospectively validated model. *Ann Intern Med* 1990; **113**: 495–500.
8. Roth A, Wiklund AE, Pålsson AS *et al*. Reducing blood culture contamination by a simple informational intervention. *J Clin Microbiol* 2010; **48**: 4,552–4,558.
9. Washer LL, Chenoweth C, Kim HW *et al*. Blood culture contamination: a randomized trial evaluating the comparative effectiveness of 3 skin antiseptic interventions. *Infect Control Hosp Epidemiol* 2013; **34**: 15–21.
10. Chesnutt BK, Zamora MR, Kleinpell RM. Blood cultures for febrile patients in the acute care setting: too quick on the draw? *J Am Acad Nurse Pract* 2008; **20**: 539–546.
11. Snyder SR, Favoretto AM, Baetz RA *et al*. Effectiveness of practices to reduce blood culture contamination: a Laboratory Medicine Best Practices systematic review and meta-analysis. *Clin Biochem* 2012; **45**: 999–1,011.
12. Gander RM, Byrd L, DeCrescenzo M *et al*. Impact of blood cultures drawn by phlebotomy on contamination rates and health care costs in a hospital emergency department. *J Clin Microbiol* 2009; **47**: 1,021–1,024.
13. Chen Y, Nitzan O, Saliba W *et al*. Are blood cultures necessary in the management of women with complicated pyelonephritis? *J Infect* 2006; **53**: 235–240.
14. Henke PK, Polk HC. Efficacy of blood cultures in the critically ill surgical patient. *Surgery* 1996; **120**: 752–758.
15. Zwang O, Albert RK. Analysis of strategies to improve cost effectiveness of blood cultures. *J Hosp Med* 2006; **1**: 272–276.
16. Little JR, Murray PR, Traynor PS, Spitznagel E. A randomized trial of povidone-iodine compared with iodine tincture for venipuncture site disinfection: effects on rates of blood culture contamination. *Am J Med* 1999; **107**: 119–125.
17. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization. The true consequences of false-positive results. *JAMA* 1991; **265**: 365–369.