

DOES 2 ML BLOOD SAMPLE IN BACT/ALERT BLOOD CULTURE VERSUS 1 ML INCREASES YIELD OF ORGANISMS IN PREVIOUSLY ANTIBIOTIC-TREATED NEONATES OF MORE THAN 30 WEEKS GESTATION

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ABSTRACT

Background: The problem in NICU is that outborn neonates referred to us usually come after receiving multiple antibiotics. Now we do not have neonatal blood culture (Bact /ALERT) bottles. We send blood culture in paediatric Bact /ALERT bottles. For proper blood to broth ratio, 2 ml blood sample should be taken in paediatric Bact /ALERT bottles. The previously antibiotic-treated neonates usually have low colony counts and due to the inhibitory effects of antibiotics, cultures usually come negative. If we use proper dilutions of the blood sample and culture media to reduce the antibacterial effect, it is expected to increase the yield of organisms in previously antibiotic-treated neonates. **Method:** All extramural neonates > 30 weeks gestation admitted in NICU having clinical features and signs of neonatal sepsis and with prior exposure to antibiotics were enrolled. With all sterile precautions, paired blood culture samples of 2 ml and 1 ml were taken. **Result:** The number of total blood culture positives were 40 out of 140 cultures. Blood culture positivity was 28.6%. 30 blood cultures were common in both 2 ml and 1 ml blood samples while 10 were positive in 1 ml blood samples and another 10 in 2 ml blood samples. The value of kappa is 0.65 which shows substantial agreement between the two samples. **Conclusion:** Our study suggests that in previously antibiotic-treated neonates, increasing volume of blood in the BacT/ALERT system neither lead to an increase in yield of organisms nor do any decrease in the isolation time

Keywords: previously antibiotic-treated neonates, BacT/ALERT blood culture

INTRODUCTION

Neonatal sepsis is responsible for a considerable amount of morbidity and mortality. According to WHO estimates, there are 5 million neonatal deaths a year, 98% of which occur in the developing countries of which sepsis is the commonest cause of mortality responsible for 30-50% of neonatal deaths each year. (1,2)

Blood culture to isolate the offending pathogen remains the gold standard for the definitive diagnosis of septicemia.

The ability to exclude based on a negative blood culture result depends on the sensitivity and negative

predictive value of this test. Many factors influence the yield from blood cultures. It depends upon the method of blood culture (automated versus manual), use of previous antibiotics and colony-forming units (CFU) of organisms per ml of blood. But the single most important factor is blood volume. Evidence from both adult and paediatric studies show that the rate of isolation from blood cultures increases with the quantity of blood submitted (3-7)

The problem in NICU is that outborn neonates referred to us usually come after receiving multiple antibiotics. In these babies blood cultures usually

come negative due to prior antibiotics. In them, we are left with no choice but to use broad-spectrum antibiotics, which besides increasing the cost of treatment favours the selection of antibiotic-resistant organisms and the risk of fungal sepsis.

Now we do not have neonatal blood culture (Bact /ALERT) bottles. We send blood culture in pediatric Bact /ALERT bottles. For proper blood to broth ratio, it is the manufacturer's recommendation to take a 2 ml blood sample in pediatric Bact /ALERT bottles. The previously antibiotic-treated neonates usually have low colony counts and due to the inhibitory effects of antibiotics, cultures usually come negative. By convention, 1 ml of blood is taken for blood culture. (8,9). If we use proper dilutions of a blood sample and culture media to reduce the antibacterial effect, it is expected to increase the yield of organisms in previously antibiotic -treated neonates.

We did this observational analytical study in the Department of Neonatology, Mahatma Gandhi Medical College, Jaipur. Our primary objective was to compare the yield of organisms in 1 ml v/s 2 ml blood samples in pediatric BacT/ALERT blood culture system in previously antibiotic-treated neonates. We also looked into the time taken in isolating organisms between the two samples.

METHODOLOGY

All extramural neonates > 30 weeks gestation admitted in NICU having clinical features and signs of neonatal sepsis and with prior exposure to

antibiotics were enrolled. We excluded neonates with congenital malformations. After admitting to NICU, informed consent was taken from parents to take an extra blood sample for blood culture. History of various risk factors and antibiotics received were taken. Clinical signs of sepsis were recorded. With all sterile precautions, paired blood culture samples of 2 ml and 1 ml were taken.

RESULTS

A total of 140 neonates who previously received antibiotics were enrolled. The number of total blood culture positives were 40 out of 140 cultures. Blood culture positivity was 28.6%. 30 blood cultures were common in both 2 ml and 1 ml blood samples while 10 were positive in 1 ml blood samples and another 10 in 2 ml blood samples. The value of kappa is 0.65 which shows substantial agreement between the two samples.

In 1 ml blood culture samples, 39 (97.5%) blood cultures were positive within 1.69 days except 1 (2.5%) at 4.2 days while in 2 ml blood culture samples, 36 (90%) blood cultures were positive within 2 days except 4 (10%). The difference between blood culture positivity was not statistically significant. (p = 1.0).

Meantime to culture positivity in 1 ml blood culture samples was 0.24 days (95% CI: 0.15-0.33 days) and in 2 ml blood culture samples, mean time to culture positivity was 0.39 days (95% CI: 0.24 -0.54 days) which was also not statistically significant (p =0.038).

Blood culture profile

	1 ml sample	2ml sample	P-value	Either of them positive
Blood culture positives				
Both culture positive	30	30		
1ml sample positive	10			
2ml sample positive		10		
Total positives	40 (28.6%)	40 (28.6%)		50 (35.7%)
Blood culture positive in 48 hours	37(97.5%)	36 (90%)	1.0	
Mean time to culture positivity	0.24 days (0.15-0.33 days)	0.39 days (0.24-0.54 days)	0.038	

DISCUSSION

In our study, total blood culture positives were 50 out of 140 paired cultures. Blood culture positivity was 35.7%. 40 blood cultures were positive in either 1ml or 2 ml blood samples. Blood culture positivity in either of samples was 28.6%. In studies overall, 30% neonates clinically suspected to have LOS in an NICU setting have positive blood culture. **(10)** Thus, in our study, by increasing the amount of blood in blood culture bottles, we were able to increase the yield of organisms but it was not statistically significant

30 blood cultures were common in both 2 ml and 1 ml blood samples while 10 were positive in 1 ml blood samples and another 10 in 2 ml blood samples. Statistical test of agreement (Value of kappa is 0.65) showed substantial agreement.

The failure of one type of blood culture, but not another, to detect a pathogen could result from low level bacteremia (and the random inoculation of small numbers of microorganisms into only one of the two types of samples used).

In the adult population, in one study (1989), 17% more clinically significant isolates were detected when 13 to 16 mL of blood was cultured, in contrast to 6.5 to 8 mL **(4)** Several studies in adults have confirmed the increase in detection rates that result from increased blood culture volume, reporting figures of 0.6% to 4.7% increased yield for each extra 1 mL of blood cultured. **(5,14, 11)**

In the pediatric population, a study of 300 children attending an emergency department reported an increased yield with a single 6-mL blood culture, compared with 2 separate 2-mL cultures. In that study, up to 10 mL of blood was drawn from each individual patient, allowing a within-patient comparison of different blood volumes. **(6)** In a study of immunocompromised children, the introduction of a policy to increase blood culture volume led to an increase in the number of significant isolates recovered. **(15)** Issacman et al. **(6)** showed that increasing volume of blood improves timely detection of bacteremia in pediatric (>2 months) in Bactec system. Schelonca et al. **(9)** showed that 2 ml blood in BacT/ALERT increases organism recovery in face of low colony counts (1-3 cfu/ml). In a recent study of Kenyan children, there was an increase in the blood culture isolation rate with increasing volume, from 5.6% at 1 mL to 6.8% at 2 mL and 7.9% at 3 mL. **(12)**

In contrast, there was no difference in overall isolation rates between 0.5-mL and 1.5-mL blood cultures (13.4% vs 13.1%) in a recent study that investigated 2 blood culture procedures in a PICU. However, coagulase negative staphylococci were isolated more commonly with the low-volume blood culture system, and it was not possible to determine whether they were significant or contaminant isolates. **(13)**

Thus, our study concluded that in previously antibiotic treated neonates, increasing volume of blood in BacT/ALERT system neither led to increase in yield of organisms nor there was any decrease in the isolation time.

Though, it can be suggested that taking two samples lead to isolation of more organisms than one sample alone.

There are many potential clinical advantages of inoculating two or more culture per patient. These advantages include a possible increase in the number of infants from whom pathogens can be detected and assistance either with the selection of more specific antimicrobial agents when the pathogen is detected or with the discontinuation of unnecessary therapy when a sensitive culture system remains negative.

Strengths and limitation of the study

The major strength of our study was that we were able to compare yield of organisms and exact time of isolation of organisms in an automated blood culture system. The major limitation of our study is that we were not able to enroll required number of neonates due to limited availability of blood culture bottles, which could have affected the statistical significance. Another limitation was that we could not do serum antibiotic levels as well as estimation of colony forming units (cfu) of organisms.

CONCLUSION

Our study suggests that in previously antibiotic treated neonates, increasing volume of blood in the BacT/ALERT system neither lead to an increase in yield of organisms nor do any decrease in the isolation time.

Though, it can be suggested that taking two samples lead to the isolation of more organisms than one sample alone.

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