JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 1993, p. 734–735
0095-1137/93/030734-02$02.00/0

Vol. 31, No. 3

Effectiveness of Resins in Removing Antibiotics from Blood Cultures

O. CREPIN, M. ROUSSEL-DELVALLEZ, G. R. MARTIN, AND R. J. COURCOL*

Bacteriology Laboratory, A. Calmette Hospital, 59037 Lille Cedex, France

Received 5 May 1992/Accepted 23 November 1992

The present study evaluates the effectiveness of BACTEC NR-26A resin-containing medium in removing eight antibiotics from blood cultures. Peak concentrations achievable clinically were chosen. All antibiotics were prepared in fresh human blood samples. Blood samples were obtained prior to and at 15 min and 2, 24, 48, and 72 h after inoculation. Aztreonam, ceftriaxone, imipenem, teicoplanin, and ticarcillin were partially removed from blood cultures.

Bacterial growth can be suppressed or slowed in vials containing blood cultures that were inoculated with blood samples from patients receiving antibiotics. Anionic and cationic resins have been proposed and incorporated into vials containing blood cultures to remove antibiotics and therefore to enhance the recovery of bacteria (2, 3, 6, 8–11). For instance, Lindsey and Riely (6) measured the removal of 13 antibiotics and 3 antibiotic combinations by the Antimicrobial Removal Device (ARD) (Marion Scientific, Kansas City, Mo.). They concluded that the ARD removed antibiotics such as beta-lactams, aminoglycosides, tetracycline, and sulfamethoxazole. The presence of resins did not interfere with bacterial growth. In a previous study, we reported that BACTEC NR-16A resin-containing medium recovered significantly more bacteria than did BACTEC NR-6A non-resin-containing medium (2). Moreover, the mean detection time was shorter with aerobic resin-containing medium. However, we emphasized the need to check the removal of each new antimicrobial agent with vials containing medium and resins. Since this report, several antibiotics have been marketed and routinely used in practice. The present study evaluates the effectiveness of BACTEC NR-26A resin-containing medium (Becton-Dickinson Instrument Systems, Towson, Md.) to remove eight common antibiotics from human blood.

Eight antibiotics were tested: aztreonam (Bristol Myers Squibb Laboratories), cefotaxime (Hoechst-Roussel Laboratories), ceftizoxime (Pharmuka Laboratories), ceftriaxone (Roche Laboratories), ciprofloxacin (Bayer Laboratories), imipenem (Merck Sharp Dohme Laboratories), teicoplanin (Merrell Dow Laboratories), and ticarcillin (Beecham Laboratories). All antibiotic solutions were prepared from powders of certified potency and used the same day. The following antibiotic concentrations were chosen to fall within a clinically achievable range: 150 μg/ml for aztreonam; 80 μg/ml for imipenem, cefotaxime, ceftizoxime, and ceftriaxone; 5 μg/ml for ciprofloxacin; 70 μg/ml for teicoplanin; and 200 μg/ml for ticarcillin. Forty milliliters of fresh human blood was drawn from a healthy donor (O.C.). Antibiotic solution was added into the blood sample to obtain the assigned concentration. Thereafter, 10-ml portions of blood were injected into three BACTEC NR-26A vials containing 25 ml of medium with resins. The 10 ml remaining was used as the control. Vials were placed on the BACTEC orbital shaker (300 rpm) for 24 h. Samples were obtained prior to and at 15 min and 2, 24, 48, and 72 h after inoculation. Antibiotics added to human blood were diluted, giving an initial concentration in the vial at 0 min. Concentrations of antibiotics were determined in triplicate by the microbiological method (4), except that teicoplanin concentrations were determined by using fluorescence polarization immunoassay technology (International BioClinical Inc., Portland, Oreg.). The results were given as the mean values of three determinations from three bottles containing blood cultures. The decline in antibiotic concentration was expressed as a percentage of the original concentration [(measured value/intended value) × 100].

Table 1 shows the remaining activities of each antibiotic. Cefotaxime, ceftizoxime, and ciprofloxacin were completely removed after 15 min. In contrast, the activities of the other antibiotics were partly reduced. This phenomenon was observed especially for aztreonam, imipenem, teicoplanin, and ticarcillin. The remaining activities of these four antibiotics at 2 h were 35.7, 89.6, 17.3, and 22.7%, respectively. The antibiotic concentrations were greater than the susceptible breakpoints for imipenem (20.0 μg/ml) 2 h after inoculation and for aztreonam (9.8 μg/ml) 48 h after inoculation. For teicoplanin and ticarcillin, the remaining activities were sufficiently high to delay the bacterial growth.

This study shows that BACTEC NR-26A blood culture resin medium may be inefficient for removal of clinically achievable concentrations of potent antibiotics which are prescribed to treat acutely infected patients. Therefore, microorganisms causing bacteremia might fail to grow in BACTEC NR-26A medium in patients receiving the recently marketed antibiotics mentioned earlier. These results are in complete agreement with researchers who found that generally resin-containing medium had no advantage over the conventional vials with blood cultures (3, 8, 9, 11). As reported by Lindsey and Riely (6) with the ARD, we also found a residual activity with ticarcillin. Antibiotic concentrations were equivalent, except for the type of the resins in the medium. Moreover, our results are in agreement with those reported by Bartley et al. (1) about the remaining activities of aztreonam and imipenem in BACTEC NR-16B vials.

Despite their inefficiency in removing some antibiotics,

* Corresponding author.

TABLE 1. Mean concentrations of antibiotics in BACTEC NR-26A medium and remaining antibiotic activities

Antimicrobial agent and time after inoculation	Mean concentration (μg/ml)	Remaining activity (%)	MIC breakpoint (≤μg/ml)
Aztreonam			8
0 min	42.8		
15 min	28.0	65.4	
2 h	15.3	35.7	
24 h	13.5	31.5	
48 h	9.8	22.9	
72 h	4.0	9.4	
Cefotaxime			8
0 min	19.7		
15 min	0	0	
Ceftizoxime			8
0 min	25.0		
15 min	0	0	
Ceftriaxone			8
0 min	17.1		
15 min	5.8	33.9	
2 h	2.9	16.9	
24 h	0.8	4.6	
48 h	0	0	
Ciprofloxacin			1
0 min	1.4		
15 min	0	0	
Imipenem			4
0 min	22.3		
15 min	19.8	88.7	
2 h	20.0	89.6	
24 h	2.3	10.3	
48 h	1.9	8.5	
72 h	0	0	
Teicoplanin			4
0 min	21.9		
15 min	4.7	21.5	
2 h	3.8	17.3	
24 h	3.5	15.9	
48 h	3.3	15.0	
72 h	2.1	9.6	
Ticarcillin			16
0 min	57.1		
15 min	21.6	37.8	
2 h	13.0	22.7	
24 h	3.6	6.3	
48 h	0	0	

resins in blood culture medium could increase the recovery of microorganisms because of the lysis of leukocytes, as demonstrated by Jungkind et al. (5). Moreover, the 10-ml volume of blood inoculated into the BACTEC NR-26A vial (compared with 3- to 5-ml volumes of blood inoculated into conventional BACTEC vials) is also an important factor in enhancing the recovery of microorganisms from this medium. Finally, our results emphasize that even with the use of resin-containing medium, blood cultures are best drawn when antimicrobial concentrations are at their lowest levels, as recommended by Rodriguez and Lorian (7).

REFERENCES

1. **Bartley, C., M. Secrist, L. Mui, and N. Sullivan.** 1992. Evaluation of the resin technology for inactivation of antibiotics in blood cultures, C-83, p. 434. Abstr. 92th Gen. Meet. Am. Soc. Microbiol. 1992. American Society for Microbiology, Washington, D.C.
2. **Courcol, R. J., A. V. Durocher, M. Roussel-Delvallez, A. Fruchart, and G. R. Martin.** 1988. Routine evaluation of BACTEC NR-16A and NR-17A media. J. Clin. Microbiol. **26**:1619–1622.
3. **DeGirolami, P. C., K. Eichelberger, and J. Siegel.** 1984. Detection of bacteremia with the BACTEC 16B resin blood culture medium. Am. J. Clin. Pathol. **81**:643–646.
4. **Grove, D. C., and W. A. Randall.** 1955. Assay methods of antibiotics: a laboratory manual. Antibiotics monograph 2. Medical Encyclopedia, New York.
5. **Jungkind, D. L., M. Thakur, and J. Dyke.** 1989. Evidence for a second mechanism of action of resin in BACTEC NR-16A aerobic blood culture medium, C-225, p. 431. Abstr. 89th Annu. Meet. Am. Soc. Microbiol. 1989. American Society for Microbiology, Washington, D.C.
6. **Lindsey, N. J., and P. E. Riely.** 1981. In vitro antibiotic removal and bacterial recovery from blood with an antibiotic device. J. Clin. Microbiol. **13**:503–507.
7. **Rodriguez, F., and V. Lorian.** 1985. Antibacterial activity in blood cultures. J. Clin. Microbiol. **21**:262–263.
8. **Strand, C. L.** 1982. Evaluation of the antimicrobial removal device when used with the BACTEC blood culture system. Am. J. Clin. Pathol. **78**:853–856.
9. **Tegtmeier, B. R., and J. L. Vice.** 1984. Evaluation of the BACTEC 16B medium in a cancer center. Am. J. Clin. Pathol. **81**:783–786.
10. **Weinstein, M. P., S. Mirrett, M. L. Wilson, L. J. Harrell, C. W. Stratton, and L. B. Reller.** 1991. Controlled evaluation of BACTEC Plus 26 and Roche Septi-Check aerobic blood culture bottles. J. Clin. Microbiol. **29**:879–882.
11. **Wright, A. J., R. L. Thompson, C. A. McLimans, W. R. Wilson, and J. A. Washington II.** 1982. The antimicrobial removal device: a microbiological and clinical evaluation. Am. J. Clin. Pathol. **78**:173–177.