Prophylactic Antibiotics in Neonates with Umbilical Artery Catheter Placement
A Prospective Study of 137 Patients

RICHARD M. COWETT, GEORGES PETER, DAVID O. HAKANSON, LEO STERN, AND WILLIAM OH
Brown University Program in Medicine, Providence, Rhode Island
Received November 1, 1976

To analyze the risk of cannula sepsis from indwelling umbilical arterial catheters and the indication for prophylactic antibiotics, 137 catheterized neonates with respiratory distress were prospectively placed into either antibiotic-treated (penicillin 50,000U/kg/day and kanamycin 15 mg./kg./day) or non-treated groups. Although bacteria were frequently isolated from blood and catheter tip cultures obtained upon removal of the catheter, especially among non-antibiotic treated infants, these isolates were predominantly non-pathogens and probably skin flora. Corresponding peripheral blood cultures were usually sterile. No cases of cannula-associated sepsis occurred among treated and non-treated newborns. The risk of bacteriologically proven sepsis resulting from an indwelling umbilical artery catheter appears insufficient to justify prophylactic antibiotics.

The greater susceptibility of newborn infants to bacterial infection and the potential portal of entry for bacteria provided by an indwelling umbilical artery catheter has resulted in the use of prophylactic antibiotics in some nurseries for infants with these catheters [1]. Since the management of seriously ill newborns frequently necessitates umbilical artery catheterization either for blood gas determination or for fluid administration, this practice increases the use of antibiotics in intensive care nurseries. Since the emergence of resistant Gram-negative enteric bacteria has been related to antimicrobial usage [2-4], prophylaxis should not be undertaken without evidence of efficacy.

Previous studies have suggested that the risk of cannula sepsis from an umbilical artery catheter is low [5,6], but the continued use of prophylactic antibiotics in this circumstance indicates the need for further prospective studies of the risk of infection. This investigation compares this risk from indwelling umbilical arterial catheters in 83 newborns who received antibiotics with that in 54 non-treated infants.

MATERIALS AND METHODS

Patients

From January 15, 1974, to April 15, 1975, newborn infants admitted to the Special Care Nursery of the Women and Infants Hospital of Rhode Island whose clinical management in the initial 24 hours of life required an umbilical artery catheter were eligible for this prospective study. This included infants born at the Women and Infants Hospital and those born at regional hospitals for which the nursery serves as

---

1Presented in part at the 15th Interscience Conference on Antimicrobial Agents and Chemotherapy, September 24-26, 1975, Washington, D.C.

Please address reprint requests to: Richard M. Cowett, M.D., 50 Maude Street, Providence, RI 02908

Copyright © 1977 by The Yale Journal of Biology and Medicine, Inc.
All rights of reproduction in any form reserved.
the tertiary care referral center. The indication for catheterization in all infants was respiratory distress. Duration of catheter placement in each infant was determined by the physicians caring for the infant, independent of the study.

Catheterization Technique

Catheterizations were performed by the pediatric house staff, using standard aseptic techniques. The umbilical area was cleansed with povidone iodine solution for 3 minutes and rinsed with 70 percent alcohol. After the umbilical cord was cut 1.0 to 2.0 cm. from the skin, a polyethylene umbilical catheter (Argyl umbilical artery catheter, Sherwood Medical Industries, St. Louis, MO 63103) was inserted into the umbilical artery through the aorta to the T6-T10 vertebral level. The position of the catheter tip was confirmed by radiography. The catheter was secured by suture to the cord; Neosporin (Polymyxin B-bacitracin-neomycin ointment, Burroughs Wellcome Co., Research Triangle Park, NC 27709) or bacitracin ointment was applied and the umbilical stump covered with a dry, sterile dressing for the duration of the catheter placement.

Culture Technique

The following samples were obtained by the house staff for cultures from patients in the study within 15 minutes of placement or withdrawal of the catheter:

1. Blood from a peripheral vein prior to catheterization.
2. Blood from the umbilical artery catheter immediately after its insertion.
3. Blood from the catheter immediately before its removal.
4. Blood from a peripheral vein at time of catheter removal.
5. Upon removal of the catheter, the distal 2.0 cm. of the catheter tip was cut with sterile scissors and placed in thioglycolate broth.

For blood cultures, 0.5 to 1.0 ml. was placed in 20 ml. of Columbia broth (Scott Laboratories, Fiskeville, RI 02823). All cultures were processed by the standard techniques of the hospital’s bacteriology laboratory.

Antibiotic Administration

Infants entered into the study were placed in one of three groups depending on the time of birth.

I. Infants, born on even days of the month, received antibiotics; aqueous penicillin G 25,000 U/kg intravascularly every 12 hours, and kanamycin 5.0 mg/kg intramuscularly every 8 hours, irrespective of whether an infant required antibiotics for other reasons.

II. No antibiotics were given to infants born on odd days of the month.

III. Infants, born on odd days, whose physicians requested that antibiotics be administered because they suspected infection on the basis of clinical findings did receive antibiotics.

No attempt was made to separate infants in Group I who would have received antibiotics for other reasons beside catheter placement.

RESULTS

Of the 137 infants entered into the study, 58 were in Group I, 54 were in Group II, and 25 were in Group III. Of the latter, one infant did have Hemophilus influenzae b septicemia, one had a pustular skin eruption, and three had radiographically-
documented pneumonia. Two and three infants respectively in Groups I and II also had radiographically Documented pneumonia. Table 1 shows that the three groups of infants were similar in estimated gestational age, age at catheterization, and duration of catheterization. Whereas the mean birth weights for Groups I and II were similar, the mean birth weight of Group III (1686 gm) was significantly lower (p<0.05) than that of Group II (2036 gm). This difference reflects the non-randomized basis for the selection of infants in Group III. Paired peripheral and catheter blood cultures obtained from 113 of these infants at the time of catheter insertion demonstrated that blood obtained from an umbilical artery catheter in an infant less than 24 hours old is equally reliable as a peripheral blood culture for the diagnosis of bacteremia. Six of 113 cultures of peripheral blood yielded bacteria; two were pathogens, and four were nonpathogens. Five cultures of 113 specimens of catheter blood were positive; three were pathogens, and two were nonpathogens. Table 2 shows that the three groupsof infants were similar in estimated gestational age, age at catheterization, and duration of catheterization. Whereas the mean birth weights for Groups I and II were similar, the mean birth weight of Group III (1686 gm) was significantly lower (p<0.05) than that of Group II (2036 gm). This difference reflects the non-randomized basis for the selection of infants in Group III. Paired peripheral and catheter blood cultures obtained from 113 of these infants at the time of catheter insertion demonstrated that blood obtained from an umbilical artery catheter in an infant less than 24 hours old is equally reliable as a peripheral blood culture for the diagnosis of bacteremia. Six of 113 cultures of peripheral blood yielded bacteria; two were pathogens, and four were nonpathogens. Five cultures of 113 specimens of catheter blood were positive; three were pathogens, and two were nonpathogens. Comparison of the pathogens obtained by each route shows that two of the three pathogens obtained from catheter blood samples were identical to those obtained from the peripheral blood [7].

The results of cultures obtained at the time of catheter removal are listed in Table 2. One or more cultures were obtained from each infant, although in some cases all three of the cultures specified in the protocol were not. All of the peripheral blood cultures from infants in the antibiotic-treated groups, I and III, and 32 of 35 cultures from the non-treated infants (Group II) were sterile. Catheter blood cultures from infants in Groups I and III also were sterile, but 14 of 34 from Group II infants yielded bacteria. Cultures of the catheter tips were positive for bacterial growth in eight of 37 in Group I, 12 of 36 in Group II, and one of 25 in Group III infants. Comparison of results from Group I and those from Group II demonstrated that positive catheter blood cultures occurred significantly more often (p<0.05) in Group II than Group I. Comparison of the results from all antibiotic-treated infants (Group I and III) with those from the non-treated infants (Group II) showed that both catheter blood and tip cultures from non-treated infants yielded bacteria more frequently (p<0.05) than did those from infants receiving antibiotics.

Many of these isolates, however, were non-pathogens (Staph. epidermidis, Propionibacterium acnes, non-Group D Alpha streptococci, Micrococcus sp., and Diptheroids), not associated with signs or symptoms of infection. The recovery of pathogens is indicated by parentheses in Table 2 and occurred in only four infants, all of whom were in Group II and did not receive prophylactic antibiotics. The clinical courses of these infants were reviewed to determine if any of these cases were consistent with cannula sepsis attributable to an indwelling arterial catheter; this information is summarized in Table 3. Only one (TA) of the four was clinically symptomatic. This infant's catheter was removed after the onset of lethargy, antibiotics begun, and the infant subsequently improved. This infant had Proteus mirabilis septicemia, but since the catheter tip was sterile, the catheter cannot definitively be implicated. Defining cannula sepsis as isolation of the same organism from both the peripheral blood and catheter tip culture in conjunction with clinical manifestations of infection, none of these infants had cannula sepsis.

During hospitalization 17 of the 137 (12.4%) study infants died, including nine of 58 (15.5%) in Group I, six of 54 (11.1%) in Group II, and two of 25 (8%) in Group III. Autopsies were performed in 14 cases and none had died of infection. Twelve infants died of hyaline membrane disease. The remaining 3 non-autopsied infants died of respiratory distress syndrome with respiratory failure.
TABLE 1
Clinical Data of Patient Groups

|                     | Group I<sup>a</sup> (58) | Group II<sup>b</sup> (54) | Group III<sup>b</sup> (25) |
|---------------------|---------------------------|---------------------------|---------------------------|
| Birthweight<sup>a</sup> (gms) | 1835 ± 644.               | 2036 ± 696.               | 1686 ± 819.               |
| Gestational Age<sup>a</sup> (wks) | 33 ± 3                   | 33 ± 7                   | 32 ± 4                   |
| Age at Catheterization<sup>a</sup> (hrs) | 3 ± 2.8                  | 5 ± 4.8                  | 3 ± 3.4                  |
| Duration of Catheter in situ<sup>a</sup> (hrs) | 76 ± 53                  | 76 ± 48                  | 94 ± 63                  |
| Range               | 6.0–200                   | 15–260                   | 7.5–260                   |

<sup>a</sup>Mean ± S.D.
<sup>b</sup>Received Antibiotics

TABLE 2
Culture Results of Catheter Tip and Blood Obtained from Peripheral Vein and Umbilical Arterial Catheter (Number of pathogens recovered is shown in parentheses)

|                     | Peripheral Blood | Catheter Blood | Catheter Tip |
|---------------------|------------------|----------------|--------------|
| **Group I** (Antibiotics) |                  |                |              |
| Total Cultures      | 36               | 37             | 37           |
| Positives           | 0                | 0              | 8 (0)        |
| **Group II** (No Antibiotics) |                |                |              |
| Total Cultures      | 35               | 34             | 36           |
| Positives           | 3 (2)            | 14 (4)         | 12 (1)       |
| **Group III** (Antibiotics—Non-randomized) | | |
| Total Cultures      | 18               | 16             | 25           |
| Positives           | 0                | 0              | 1 (0)        |

TABLE 3
Culture Results and Clinical History of Four Infants from Whom Pathogens Were Recovered at Catheter Removal

| Patient | Peripheral Blood | Catheter Blood | Catheter Tip | Clinical History |
|---------|------------------|----------------|--------------|------------------|
| TA      | *Proteus mirabilis* | *Proteus mirabilis* | No growth | Lethargy         |
| CA      | *Escherichia coli* | *Escherichia coli* | *Staph. epidermidis* | Unremarkable |
| PR      | No growth        | *Escherichia coli* | *Escherichia coli* | Unremarkable |
| PA      | Not taken        | *Escherichia coli* | No growth | Unremarkable |

The incidence of bacterial growth (both pathogens and non-pathogens) from the catheter tip and the duration of the catheter in situ among antibiotic-treated and non-treated infants were compared. Among the non-treated group of infants, the incidence of colonization was greater for those catheters removed after 48 hours of use in comparison to those in place for 48 hours or less. This difference was not statistically significant.
DISCUSSION

In this prospective study of 137 newborns with an umbilical arterial catheter, no case of cannula sepsis occurred in spite of the 21 percent incidence of bacterial growth from catheter tip cultures. This disparity between catheter tip culture results and bacteremia was also noted by Bard et al. in a comparable series of 75 infants in which 39 percent of catheter tip cultures were positive [5]. These authors noted two possible cases of sepsis related to arterial catheterization; but in both infants, the peripheral blood isolate at the time of the catheter removal was not the same as the catheter tip organism. Other studies of umbilical catheters either have not obtained peripheral blood cultures in association with catheter tip cultures [8–11] or have involved only venous catheters [12–14].

The high incidence of positive catheter tip cultures in this and other studies of umbilical catheters has not been associated with cannula sepsis [5,6,8,14], and has been attributed to contamination with umbilical bacterial flora [14]. The umbilicus rapidly becomes colonized after the first 24 hours of life even in antibiotic-treated infants [15,16]. Also in support of the insignificance of catheter tip bacterial growth is that the isolated organisms have been predominantly non-pathogens [5,8,10,13,14]; only one of 21 in this series is a potential pathogen. Furthermore, the effect of antibiotics on catheter tip cultures may be misleading, since penicillin in this study was given through the catheter. Residual antibiotic in the lumen of the catheter could have suppressed in vitro growth in the culture media without eradicating a nidus of growth on the foreign body. The results of catheter blood cultures upon removal of the catheter also reflect possible contamination and/or possible residual antibiotic, and do not justify prophylactic antibiotics.

This and previous studies do not support the value of prophylactic antibiotics for catheterized infants [5,6,8,14]. The design of this study, however, does not exclude the possibility that some infants might benefit from prophylactic antibiotics. For example, the infants who received antibiotics at the request of their physicians might have been at higher risk of infection than those infants remaining in Group II who did not receive antibiotics, and, thus, have benefited from prophylactic antibiotics. The lower birthweight of these infants lends credence to this possibility. Furthermore, since the antibiotic-treated Group I included some infants whose physicians would have given antibiotics for suspected infections irrespective of the time of birth, akin to Group III, antibiotics might have prevented infection in these infants as well as those in Group III. The creation of Group III may have obscured a possible advantage of prophylactic antibiotics. To date, however, no umbilical catheter study has identified a subset of infants with catheters for whom prophylactic antibiotics are of benefit. Further studies with larger numbers and strict randomization of patients are needed to determine the characteristics of those, if any, infants who might benefit from prophylactic antibiotics.

Without evidence of efficacy, prophylactic antibiotics in newborn nurseries should be avoided. High rates of colonization with enteric bacilli multi-resistant to antimicrobials have been observed in premature nurseries where kanamycin was used extensively [2–4]. Baker et al. found an increased incidence of resistance to kanamycin and ampicillin among E. coli isolates from infants with either prior antibiotic therapy and/or prolonged hospitalization [4].

The low incidence of infectious complications associated with umbilical arterial catheters in this and other studies does not minimize the potential hazard incurred with an indwelling vascular catheter. Vascular complications including thrombosis,
ischemia, hemorrhage, and embolism are well documented [17]. Furthermore, the low incidence of infection does not preclude nosocomial bacteremia. A recent outbreak among adults of Flavo-bacterium species bacteremia attributed to contaminated arterial catheters attests to this continuing risk with any arterial cannula [18]. Proper management of the high risk newborn should include careful aseptic techniques for catheterization, avoidance of unnecessary catheter manipulation, and removal as soon as possible, but not prophylactic antibiotics.

ACKNOWLEDGEMENT

We are indebted to the staff of the Diagnostic Bacteriology Laboratory of Women and Infants Hospital of Rhode Island, Mrs. Barbara Davis, R.N., and Mrs. Jane Dempsey, R.N., as well as the Pediatric House Staff.

REFERENCES

1. Kitterman JA, Phibbs RH, Tooley WH: Catheterization of umbilical vessels in newborn infants. Ped Clin N A 17:895–912, 1970
2. Eisenach KD, Reber RM, Eitzman DV, et al: Nosocomial infections due to kanamycin-resistant, (R)-factor carrying enteric organisms in an intensive care nursery. Ped 50:395–402, 1972
3. Franco JA, Eitzman DV, Baer H: Antibiotic usage and microbial resistance in an intensive care nursery. Am J Dis Child 126:318–321, 1973
4. Baker CJ, Barrett FF, Clark DJ: Incidence of kanamycin resistance among Escherichia coli isolates from neonates. J Ped 84:126–130, 1974
5. Bard H, Albert G, Teasdale F, et al: Prophylactic antibiotics in chronic umbilical artery catheterization in respiratory distress syndrome. Arch Dis Child 48:630–635, 1973
6. van Vliet PKJ, Gupta JM: Prophylactic antibiotics in umbilical artery catheterization in the newborn. Arch Dis Child 48:296–300, 1973
7. Cowett RM, Peter G, Hakanson DO, et al: Reliability of bacterial culture of blood obtained from an umbilical artery catheter. J Ped 88:1035–1036, 1976
8. Krauss AN, Albert RF, Kannan, MM: Contamination of umbilical catheters in the newborn infant. J Ped 77:965–969, 1970
9. Casalino MB, Lipsitz PJ: Contamination of umbilical catheters (letter). J Ped 78:1077–1078, 1971
10. Powers WF, Tooley WH: Contamination of umbilical vessel catheters: Encouraging information (letter). Ped 49:470–471, 1972
11. Symansky MR, Fox HA: Umbilical vessel catheterization: Indications, management, and evaluation of the technique. J Ped 80:820–826, 1972
12. Nelson JD, Richardson J, Shelton S: The significance of bacteremia with exchange transfusions. J Ped 66:291–299, 1965
13. Balagtas RC, Bell CE, Edwards LD, et al: Risk of local and systemic infections associated with umbilical vein catheterization: A prospective study in 86 newborn patients. Ped 48:359–367, 1971
14. Anagnostakis D, Kamba A, Petrochilou V, et al: Risk of infection associated with umbilical vein catheterization. J Ped 86:759–765, 1975
15. Fairchild JP, Graber CD, Vogel EH, et al: Flora of the umbilical stump. J Ped 53:538–546, 1958
16. Oh W, Keller R, Klein RI, et al: Antibiotics in infants for premature rupture of membranes. Am J Dis Child 108:149–153, 1964
17. James LS: Complications arising from catheterization of the umbilical vessels. In Problems of Neonatal Intensive Care Units Report of the Fifty-Ninth Ross Conference on Pediatric Research. p 37, 1969
18. Stamm WE, Colella JJ, Anderson RL, et al: Indwelling arterial catheters as a source of nosocomial bacteremia. New Eng J Med 292:1099–1102, 1975
Richard M. Cowett, M.D.
Georges Peter, M.D.
David O. Hakanson, M.D.
Leo Stern, M.D.
William Oh, M.D.

Departments of Pediatrics
Women and Infants Hospital of Rhode Island
and
Roger Williams General Hospital
and
Section of Reproductive and Developmental Medicine
Brown University Program in Medicine
Providence, Rhode Island