Antibiotic Lock Technique: A Review of the Literature

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OBJECTIVE: To review the literature on the use of the antibiotic lock technique (ALT) as a treatment option for patients with highly needed catheters.

DATA SOURCES: MEDLINE and *International Pharmaceutical Abstracts* were searched (1980–August 2004). Search terms included antibiotic lock, catheter infection, and topical treatment.

STUDY SELECTION AND DATA EXTRACTION: Articles describing use of ALT in the treatment of catheter infections in humans and studies evaluating in vitro stability of antibiotics were included.

DATA SYNTHESIS: ALT has been used in patients with highly needed catheters, usually for parenteral nutrition, cancer chemotherapy, or dialysis. Catheters are considered highly needed when removal is not feasible or desirable due to lack of alternative injection sites for required therapy. Success rates in saving the infected catheter have been variable and may depend on the infecting organism. In addition, there are conflicting data in terms of compatibility of antibiotics with heparin solutions.

CONCLUSIONS: Consensus appears to be that the ALT can be tried for patients with highly needed catheters when infection with coagulase-negative staphylococci is documented and no systemic signs of sepsis, such as hypotension, are evident. Most of these patients are likely to need systemic therapy as well. Infection of the catheter associated with systemic gram-negative bacteremia or fungemia will most likely require removal of the catheter to prevent systemic complications. Additional research with the ALT is warranted given unanswered questions.

KEY WORDS: catheter infection, topical antibiotic.

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Central and peripheral venous catheters are used in >50% of hospitalized patients, with >5 million central venous catheters inserted each year.[1,2] Tunneled central venous catheters are usually surgically implanted and are used to provide prolonged access for patients needing dialysis, cancer chemotherapy, or parenteral nutrition. Common types of tunneled central venous catheters are Broviac, Hickman, Groshon, and Quinton. In contrast, totally implanted intravenous access devices have a subcutaneous pocket or reservoir and are commonly referred to as ports.[3-5] It is estimated that >120 000 catheter-related bloodstream infections (CRBSIs) occur annually in hospitalized patients.[5,6] The estimated mortality rate associated with these infections is 10–20%, with a marginal cost to the healthcare system of up to $40 000 per episode.[6] The commonly accepted definition of CRBSI requires that both peripheral vein and catheter site cultures grow the same organism.[7-9]

Two risk factors for catheter-related infections that have been identified are the material of which the device is made and the intrinsic virulence of the infecting organism(s).[5,9] Catheters made of teflon or polyurethane have been reported to result in fewer infections than those made of polyvinyl chloride or polyethylene.[5] Coagulase-negative staphylococci are the most common cause of hospital-acquired CRBSIs. The initial bacterial adhesion to the catheter depends on bacteria–biomedical surface interactions including Van der Waals forces, electrostatic interactions, and hydrophobic interactions.[10] Once attached, *Staphylococcus epidermidis* and other staphylococci produce extra-

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cellular biofilm, which acts to protect bacteria against host defenses and antimicrobial agents.[5,10,11] It has been reported that antimicrobial concentrations >100–1000 times the concentration needed to kill the bacteria in solution are required to eradicate bacteria in biofilm.[1]

The 3 main types of catheter infection are exit site infection with drainage; tunnel infection with induration, tenderness, and erythema around the catheter site; and device-related bacteremia when blood cultures drawn from both the catheter and peripheral sites grow the same organism.[12-15] Most literature reports about the antibiotic lock technique (ALT) describe patients with the latter type of infection. It is important to draw blood specimens for both catheter and peripheral site cultures. Cultures of blood drawn through the catheter alone may grow a variety of organisms that colonize the site, but are not the cause of true CRBSIs. Growth from peripheral sites alone cannot differentiate between transient bacteremias and a true CRBSI.[8]

Management of the infection depends on the type of catheter, the infecting organism, and the patient's status.[1] Usually, catheter removal is the treatment of choice, especially for infections caused by gram-negative rods.[15,16] Highly needed catheters are defined as tunneled central venous catheters and totally implanted devices or ports for patients who require long-term parenteral nutrition or dialysis and catheters used in patients with AIDS or cancer who need to receive chronic intravenous medications.[1,10,17,18] The major threat of infection due to long-term catheter placement is intraluminal migration of bacteria from the catheter hub[1,6,11,19]; hence, the ALT was developed. The ALT is essentially a salvage technique usually reserved for patients in whom intravenous access is difficult to establish and who typically need long-term intravenous access.

Antibiotic Lock Technique

The ALT consists of filling the lumen of the catheter with antibiotic at concentrations 100- to 1000-fold higher than usual target systemic concentrations and allowing it to dwell (lock) for a period of time while the catheter is not in use in order to sterilize it.[1,17,18] Some clinicians prefer a 24-hour dwell time, which may not be possible for patients requiring additional therapies using the catheter.[11] Attempting to salvage current catheters seeks to avoid the risks, time, costs, and inconveniences associated with replacement of implanted catheters, which is often performed in the operating room.[1,20] Advantages of the ALT are decreased risk of antibiotic adverse effects due to negligible systemic concentrations if no systemic therapy is used concomitantly, increased local concentrations at the infection site, ease of administration, and ability to administer in the outpatient setting.[11,14,17,21] It is also possible that the ALT would offer cost-savings compared with replacing the catheter as a surgical procedure or needing parenteral systemic therapy; this has been a main incentive in attempting ALT to salvage catheters. Krzywda et al.[22] reported average cost-savings of 87% by using the ALT ($8.53 per day) compared with conventional parenteral antibiotic therapy ($64.17 per day) in 19 episodes of central venous catheter infection. Some disadvantages of the ALT include the lack of activity against organisms at distant sites; paucity of clinical data, including compatibility of antibiotics with heparin; and possible delay in curing the infection if the ALT fails.[1] Delaying cure of the infection may result in systemic bacteremia and potential for septic shock and other complications.[23] Successful ALT has been defined in most case series as negative follow-up cultures a few days after completion of a 14-day treatment course.[17,24-26] However, it has been recommended that successful catheter salvage with the ALT be defined as use of the device for at least 3 months after the initial prescription.[27]

Due to paucity of data in the pharmacy literature regarding the ALT, a review of published studies and reports was conducted to assess the level of evidence addressing the benefits and risks of the ALT.

Data Sources

A systematic search of MEDLINE and *International Pharmaceutical Abstracts* (1980–August 2004) databases for English-language reports was performed to identify publications describing use of the ALT. Search terms included antibiotic lock, catheter infection, and topical treatment. Citations were evaluated for inclusion in the review using title and abstract. Bibliographies of reports were reviewed to identify additional references.

Table 1 presents a summary of cases from reports identified in the search.[12-14,17,20,21,23-26, 28-38] A total of 383 patients have received the ALT, with 295 (77%) reported as successful. However, treatment success was not equally defined in all cases, different antibiotics and concentrations were used, and at least 70% of patients received concomitant systemic antibiotics.

Parenteral Nutrition

The majority of published experience with ALT comes from small case series in patients receiving home parenteral nutrition via tunneled catheters. The first identified description of ALT was in 22 patients with a variety of gram-positive and -negative CRBSIs.[20] In this series, only blood cultures drawn from the catheter needed to be positive. Peripheral blood cultures were not required, making it possible that patients with colonized catheters were treated and included in the analysis. Patients were treated based on the judgment of the physician. Patients were not randomly assigned to treatment and investigators were not blinded. Eleven patients were treated with short-term systemic antibiotic therapy (mean 3 days) along with ALT containing vancomycin 1 mg/mL, amikacin 1.5 mg/mL, or minocycline 0.2 mg/mL, depending on the organism isolated. An additional 11 patients were treated with the ALT alone. Solutions were allowed to dwell for 12 hours per day for 14 days.

Twenty of the catheters in this study were salvaged, 10 in each group. Two catheters required removal due to fungal infection, one in each group. The authors concluded

that there was no difference between the treatment groups. This same cohort of 22 patients was then followed for 2 years. Twenty-seven CRBSIs were treated with the ALT alone, of which 25 (93%) catheters were salvaged.[28]

Benoit et al.[29] enrolled 7 patients receiving parenteral nutrition with 9 catheter infection episodes in an open uncontrolled study. Patients with *Staphylococcus aureus* infections were excluded. Peripheral blood cultures were required. Posttreatment blood cultures were repeated only if symptoms recurred. Four patients received systemic therapy plus ALT with vancomycin 5 mg/mL, ciprofloxacin (concentration not reported), or gentamicin 5 mg/mL for

Table 1. Use of ALT for Highly Needed Catheters

Reference	ALT Indication	CRBSI Episodes Cured		Peripheral Culture Collected[a]	Systemic Antibiotics	ALT Antibiotics
		n	%			
Messing et al. (1988)[20]	PN	10	91	no	yes	vancomycin, amikacin, minocycline
		10	91	no	no	minocycline, amikacin
Messing et al. (1990)[28]	PN	25	93	no	no	vancomycin, minocycline, amikacin
Arnow et al. (1991)[32]	PN (fungal)	1	100	yes (negative)	no	amphotericin B
Doudard et al. (1991)[35]	cancer (children)	2	100	yes	yes	vancomycin, teicoplanin
		3	100	yes (negative)	no	vancomycin
Rao et al. (1992)[14]	cancer (children)	14	100	no	no	amikacin + heparin
Capdevila et al. (1993)[26]	dialysis	9	82	yes	yes	vancomycin + heparin, ciprofloxacin + heparin
Johnson et al. (1994)[21]	PN (children)	10	83	no	no	amphotericin B
Capdevila et al. (1994)[33]	AIDS	12	80	yes	no	vancomycin
Williams et al. (1994)[36]	PN	4	100	yes	yes	NR
Krzywda et al. (1995)[25]	PN	14	64	no	no	vancomycin, gentamicin, amphotericin B, cefazolin, erythromycin, nafcillin, ceftriaxone, clindamycin, ceftazidime
Benoit et al. (1995)[29]	PN	3	75	yes	yes	vancomycin, gentamicin, amphotericin B, ciprofloxacin
		3	100	yes	no	vancomycin, gentamicin
Capdevila et al. (1995)[34]	dialysis	40	100	yes	yes	NR
Bregenzer et al. (1996)[37]	cancer	1	100	NR	yes	teicoplanin
Domingo et al. (1999)[13]	AIDS	22	79	yes	unclear[b]	teicoplanin
Boorgu et al. (2000)[30]	dialysis	14	100	yes	yes	vancomycin + heparin, penicillin + heparin, piperacillin + heparin, amoxicillin + heparin
Domingo et al. (2001)[12]	AIDS	1	50	yes	yes	vancomycin
Longuet et al. (2001)[31]	AIDS, cancer	5	31	yes	yes	vancomycin, teicoplanin, amikacin
Krishnasami et al. (2002)[23]	dialysis	40	51	yes[c]	yes	vancomycin + heparin, cefazolin + heparin, gentamicin + heparin
Guedón et al. (2002)[24]	PN	15	63	yes	unclear[d]	teicoplanin
Viale et al. (2003)[17]	AIDS, cancer	15	100	yes	no	vancomycin, amikacin, teicoplanin
		13	87	yes	yes	vancomycin, amikacin, imipenem
Abraham et al. (2003)[38]	dialysis	1	100	yes	NR	vancomycin + heparin

ALT = antibiotic lock technique; CRBSI = catheter-related bloodstream infections; NR = not reported; PN = parenteral nutrition.
[a]Peripheral cultures were required to be positive when collected, unless otherwise indicated.
[b]Nine patients received concomitant systemic therapy; however, authors did not specify how many of these patients had the catheter removed; only total number was provided.
[c]No catheter cultures drawn.
[d]Twenty patients received concomitant systemic therapy; the number of these patients cured not specified.

an 8- to 12-hour dwell time. Three patients received the ALT alone. Catheters in 8 of the 9 (89%) episodes were salvaged after an average of 8.6 days of ALT and 21 days of systemic antibiotics. Duration of ALT in this study was much lower than the usual 14 days seen in most reports, and systemic therapy was given for a longer period of time, making conclusions about the usefulness of ALT alone unclear. In addition, one of the patients classified as a success received an antibiotic lock alone with gentamicin and amphotericin 2.5 mg/mL chronically for at least 250 days due to previous catheter infections that required removal of the line.

A case series report included 6 patients, most receiving parenteral nutrition, who experienced 22 episodes of CRBSIs.[25] The specific number of patients receiving parenteral nutrition was not provided. One patient accounted for 10 of the infections over a 14-month period. Three of the infection episodes were with more than one organism in this patient, including gram-negative rods and fungi. Since peripheral cultures were not performed in any patient, it is possible that some, if not all, of the episodes reported were the result of catheter colonization rather than CRBSI. Follow-up catheter specimens were cultured at the end of treatment and 2 months later to document cure. Patients received a variety of antibiotics at different doses depending on the organism(s) isolated for an average of 8 days. Of the 12 episodes in the other 5 patients, 11 (92%) were salvaged with the ALT; 9 of these episodes were due to *S. epidermidis*. However, the patient that accounted for 10 infections had 3 catheters removed and only 3 posttreatment cultures that were negative over the course of follow-up. If this patient and all 22 episodes are counted, then salvage was obtained in only 14 episodes.

One retrospective study seems to contradict positive reports of ALT use.[24] The authors reviewed the medical records of 265 patients who received parenteral nutrition through subclavian, subcutaneous tunneled catheters from January 1997 to December 1999. Catheter-related *S. epidermidis* sepsis was diagnosed if blood drawn from catheters had at least 5 times as many colony-forming units on culture as peripheral blood samples. Infected catheters were treated with a teicoplanin lock (2.5 mg/mL), with a dwell time of 12 hours daily for 14 days. During the study period, there were 24 episodes of *S. epidermidis* catheter sepsis in 14 patients. Five were hospitalized patients (5 episodes) and 9 home-care patients (19 episodes). Catheters were not removed in 15 of 24 episodes.

The authors concluded that teicoplanin ALT was not effective for *S. epidermidis* catheter-related sepsis due to their low salvage rate. Seventy-nine percent of the *S. epidermidis* isolates were methicillin-sensitive, which is rare in American hospitals today. If the glycopeptide teicoplanin is not as effective as cefazolin in methicillin-sensitive staphylococcal infections, as is the case with vancomycin, the low salvage rate could have been due to the antibiotic used rather than the lock technique. Furthermore, inpatients who likely needed short-term parenteral nutrition were included in the analysis. These patients are not likely to be considered as having highly needed catheters as parenteral nutrition therapy is not usually long term.[24]

Dialysis

Similar case series on patients receiving dialysis have been published. In a report of 11 dialysis patients with 13 bacterial CRBSIs, both catheter and peripheral cultures were required.[26] Subjects were treated with a combination of systemic antibiotics and locks for 15 days; 9 (82%) cases were successfully treated with the initial course of therapy. Patients received the ALT with vancomycin 0.1 mg/mL or ciprofloxacin 0.1 µg/mL in a 5% heparin solution with dwell time until the next dialysis period for 15 days depending on the organism isolated. Systemic antibiotics were given through the same catheter over 4 hours. Two patients had catheters that were infected with *Pseudomonas* spp., and the infection relapsed after treatment ended at 4 and 6 weeks. These 2 patients were considered cured after a second antibiotic course.

The authors reported an overall success rate of 100%. Catheters were used for an average of an additional 12.7 weeks (range 6–26) after the ALT. Eight of the lines were sterile when removed for non-infectious reasons because lines were no longer needed. Therefore, application of the ALT for use in highly needed catheters in this study is unclear given that 73% of the patients no longer needed the catheters after treatment. It was not reported whether the dialysis access was temporary while a fistula was maturing for long-term dialysis access.[26]

Another open study reported 100% success with the ALT in patients receiving dialysis via a subcutaneous access device.[30] Of 26 devices implanted, 14 bacteremic episodes were reported in 8 patients. Both catheter and peripheral cultures were required. Half of the episodes were due to *S. epidermidis*. No follow-up cultures were performed. Patients received concomitant systemic antibiotics. Locks contained a variety of antibiotics according to isolates, including vancomycin 1–3 mg/mL in a heparin solution of 100–2500 units/mL. Solutions were allowed to dwell until the next dialysis session and continued for 2–3 weeks. The authors reported that the ALT is their standard of care for bacteremic episodes with the devices. After follow-up of 329 patient-months (average 11), no devices had been removed.[30]

In contrast, a prospective open study in 79 bacteremic patients receiving dialysis showed a success rate of 51% with the ALT and systemic antibiotics.[23] Only peripheral cultures were obtained during febrile episodes. Catheters were treated throughout periods between dialysis with locks containing vancomycin 2.5 mg/mL, cefazolin 5 mg/mL, gentamicin 1 mg/mL, or a combination of these according to isolates, in addition to heparin 2500 units/mL. Systemic therapy was given with loading doses of vancomycin 20 mg/kg and gentamicin 1.5 mg/kg, followed by maintenance doses of vancomycin 500 mg and gentamicin 1 mg/kg, to a maximum of 100 mg after each dialysis session. No drug concentrations were monitored or doses adjusted, and treatment was continued for 3 weeks.

Catheter retention was prolonged by a median of 64 days. Eleven (18%) patients had serious complications from the infected catheters, including septic shock in 5 patients and endocarditis in 3 patients. Gram-negative organisms caused 6 of the 11 infections that resulted in serious complications. Sensitivities of these organisms to gentamicin were not provided. It appears that single blood cultures positive for coagulase-negative staphylococci were counted as infection even if skin contamination of the blood culture bottle was a possibility,[8] given that no catheter cultures were drawn. While the authors reported that the ALT salvaged the catheter in over half of the cases and offers clinical advantages over removing the catheter, the serious complication rate was high and increased life of the catheter was limited.[23]

Cancer or AIDS

A one-year open study was conducted in 8 children (mean age 6 y) with cancer who had 14 catheter infection episodes.[14] Patients received the ALT alone, and a 100% success rate was reported. Over half (56%) of the isolates were gram-negative rods in non-neutropenic patients. Amikacin 40 mg/mL was used in the lock containing heparin 1000 units/mL. Only catheter cultures were required. It is possible that these organisms represented colonization of the catheter site with transient bacteremias as a result of accessing the catheter rather than an infection.

Viale et al.[17] tested the ALT in an open uncontrolled study of 30 patients with bacterial CRBSIs. Forty-seven percent of patients were HIV-positive. Patients with pocket, tunnel, or secondary infections were excluded. Fifteen patients received additional systemic antibiotics, while 15 were treated with the ALT alone. Both peripheral and catheter cultures needed to be positive for the same organism to be included in the study. Patients received vancomycin 20 mg/mL, amikacin 10 mg/mL, or another antibiotic at 100 times the minimum inhibitory concentration for the isolate. The solutions were locked for at least 12 hours per day for 14 days.

The infections in 28 of 30 (93%) patients were cured, with cure defined as negative cultures from a peripheral vein and the catheter 14 days after completion of therapy. All patients treated with ALT alone were cured, as well as 13 of those receiving ALT plus systemic antibiotic therapy. The 2 patients who failed ALT had mixed infections including gram-negative isolates and received a glycopeptide antibiotic lock with combined systemic therapy. Eight of 9 *S. aureus* isolates were methicillin-resistant. The authors proposed that ALT can be an alternative to line removal/replacement in CRBSIs for HIV-positive patients.[17]

An open study limited to patients with port-related bacteremia reported a success rate of 7 of 16 (44%) patients treated with ALT and systemic therapy.[31] Ten patients were HIV-positive with CD4+ counts <30 cells/mm^3. Both catheter and peripheral cultures were required. Patients received ALT with vancomycin 5 mg/mL or teicoplanin 5 mg/mL with or without amikacin ALT (concentration not specified) according to organism(s) isolated. Patients received ALT once or twice a day depending on the antibiotic used, but no further details were provided regarding dwell time. Patients were treated for only 8 days; this may have contributed to the high failure rate. In addition, as the authors theorized, it is possible that the reservoirs of ports are not as effectively treated with the ALT as other catheter types. Furthermore, given the low CD4+ cell count of the HIV-positive patients, patients with less immunosuppression may have had different results.

Fungal Infections

While several case series have excluded patients with fungal infections,[17,23,24,26,30,31] others have reported using the ALT against fungi.[20,21,25,29,32-34] Only 3 successful cases,[21,32] 2 in pediatric patients,[21] with at least 20 failures[20,25,29,33,34] have been reported in the literature reviewed here. One successful case involved a 35-year-old man who had a catheter infection with *Malesseia furfur* and was treated with amphotericin B 2.5 mg/mL for a 12-hour dwell time per day over 21 days without systemic therapy. The patient was followed for 16 months without recurrence of infection after ALT use.[32] He had received 435 mg of systemic amphotericin B to treat a catheter infection with the same organism 2 years earlier. Both children were infected with *Candida albicans*.[21] However, no peripheral cultures were performed, and catheter colonization may have been treated in these patients. From these limited data, ALT does not appear to be useful for patients with fungal catheter infections.

Infection Prophylaxis

Using the ALT is not recommended for infection prevention because the limited data available included studies that used vancomycin-containing solutions,[39-41] and use of those solutions may increase the incidence of vancomycin-resistant enterococci.[9] Carratalá et al.[41] performed a randomized double-blind trial comparing the efficacy of heparin 10 units/mL alone (n = 57) versus vancomycin 25 µg/mL and heparin 10 units/mL (n = 60) dwelling for one hour every 2 days in preventing CRBSIs in neutropenic patients with cancer. Nine patients in the heparin arm and no patients in the heparin/vancomycin arm experienced hub colonization over the follow-up period of 35 days ($p = 0.001$). The authors concluded that the use of heparin with vancomycin is effective in preventing hub colonization with gram-positive bacteria and subsequently preventing bacteremia. Similar results were reported in 45 pediatric patients followed for a mean of 247 days.[39] However, the use of minocycline- and rifampin-impregnated catheters may be a better option for prevention of CRBSIs compared with the ALT and is the recommended strategy by the Centers for Disease Control and Prevention.[9,42]

Compatibility

Data regarding compatibility of antibiotic solutions with heparin are conflicting. The use of heparin combined with

antibiotics is theoretically necessary to increase antibiotic penetration in the fibrin sheath[43]; however, this may be more critical for catheters that are only used occasionally eg, dialysis) and therefore require prolonged dwell times[44] as opposed to catheters used for daily parenteral nutrition or antimicrobial agents. Some authors reported that heparin and vancomycin are compatible when dilute concentrations are used (eg, 0.025 mg/mL of vancomycin and 9.75 units/mL of heparin)[3,39,44] or when vancomycin <4 mg/mL and heparin 2.5–25 units/mL are employed.[30,43] Other studies have found that vancomycin 0.5 and 2 mg/mL were compatible and stable with heparin 100 units/mL.[19,45] Vancomycin 2.5 mg/mL was also shown to be compatible with 2500 units/mL of heparin.[23,30] A commonly cited study reported that vancomycin 10 mg/mL was compatible with heparin 5000 units/mL.[46] In contrast, some data suggest that high concentrations of heparin are problematic.[14]

It appears that, primarily, patients receiving dialysis with an infected catheter would require use of heparin in the lock due to expected dwell times of ≥24 hours between dialysis periods. Heparin 2500–5000 units/mL is recommended in these cases.[30,44] One study found that vancomycin 10 mg/mL given with gentamicin 5 mg/mL and heparin 5000 units/mL were compatible in vitro for 48 hours.[47] Some clinicians have reported anecdotally that, even though these concentrations have been shown to be stable, a precipitate may form when the drugs are mixed.[14] However, it appears that after light spinning, the precipitate disappears.

Guidelines

Based on the above reports and expert opinion, the Infectious Diseases Society of America (IDSA) recommends that, for uncomplicated infections of central venous catheters when catheter salvage is the goal and no tunnel infection is documented, the ALT should be used for 2 weeks.[4] The IDSA recommends this therapy for infections caused by coagulase-negative staphylococci, *S. aureus*, or gram-negative organisms. However, most of the data that appear to support use of the ALT relate to uncomplicated coagulase-negative staphylococcal infections.[1,11,17,23,24,30,48] The ALT is also recommended by the IDSA for dialysis catheters that are retained.[4] The ALT is not recommended by the IDSA or investigators for catheter infections caused by fungi.[4,11] These recommendations are mainly class B II or III or moderate evidence for conclusions.

Available evidence and opinion suggest that the ALT may be warranted in patients with an indication for catheter salvage such as a difficult-to-replace catheter, blood sterile in 48–72 hours, no signs of metastatic complications, microorganisms medically treatable, and hemodynamically stable patients.[1,5,11,17] In general, it appears that patients who should not receive the ALT include those with septic emboli, hypotension, persistent positive blood cultures, pocket infection, osteomyelitis, or endocarditis.[1,4,12,15,26]

There is a lack of well-designed, appropriately powered, randomized controlled trials in various affected populations comparing the efficacy of the ALT with the standard care of line removal with or without systemic antimicrobial therapy.[49] Several parameters remain to be defined such as usefulness of different types of antibiotics, optimum concentration, duration of treatment, patient selection, and whether systemic antibiotic therapy should be coadministered.[25,49]

Summary

Use of the ALT may be warranted in patients with highly needed catheters infected with coagulase-negative staphylococci. This technique is likely not indicated for infections in neutropenic patients until the ALT has been studied in this patient population. Due to the difficulty to eradicate *S. aureus*, *Pseudomonas* spp., or fungi with the ALT alone, catheter removal is likely warranted for these pathogens. It is not clear at this time whether the ALT should be attempted in patients who responded initially and present with recurrence of infection.

It would be prudent for providers who use ALT to audit their results and report their outcomes. Additional randomized studies are warranted, especially since many of the reports discussed in this review are small case series that are several years old and because resistance patterns and treatment options have changed over time. However, due to the low number of patients that may be available to be followed in a particular institution, these studies may be difficult to conduct unless collaborative efforts are carried out.

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References

1. Carratalá J. The antibiotic-lock technique for therapy of 'highly needed' infected catheters. Clin Microbiol Infect 2002;8:282-9.
2. Bouza E. Intravascular catheter–related infections: a growing problem, the search for better solutions (editorial). Clin Microbiol Infect 2002;8: 530.
3. Henrickson KJ, Powell KR, Schwartz CL. A dilute solution of vancomycin and heparin retains antibacterial and anticoagulant activities (letter). J Infect Dis 1988;157:600-1.
4. Mermel LA, Farr BM, Sherertz RJ, Raad II, O'Grady N, Harris JS, et al. Guidelines for the management of intravascular catheter–related infections. Clin Infect Dis 2001;32:1249-72.
5. Bouza E, Burillo A, Muñoz P. Catheter-related infections: diagnosis and intravascular treatment. Clin Microbiol Infect 2002;8:265-74.
6. Wenzel RP, Edmond MB. The impact of hospital-acquired bloodstream infections. Emerg Infect Dis 2001;7:174-7.
7. Raad I. Intravascular-catheter–related infections. Lancet 1998;351:893-8.
8. Hanna H, Raad I. Nosocomial infections related to use of intravascular devices inserted for long-term vascular access. In: Mayhall CG, ed. Hospital epidemiology and infection control. 3rd ed. Philadelphia: Lippincott, Williams & Wilkins, 2004:241-51.
9. Guidelines for the Prevention of Intravasular Catheter-Related Infections. MMWR Morb Mortal Wkly Rep 2002;51:1-29.
10. Pascual A. Pathogenesis of catheter-related infections: lessons for new designs. Clin Microbiol Infect 2002;8:256-64.

11. Berrington A, Gould FK. Use of antibiotic locks to treat colonized central venous catheters. J Antimicrob Chemother 2001;48:597-603.
12. Domingo P, Fontanet A. Management of complications associated with totally implantable ports in patients with AIDS. AIDS Patient Care STDS 2001;15:7-13.
13. Domingo P, Fontanet A, Sánchez F, Allende L, Vazquez G. Morbidity associated with long-term use of totally implantable ports in patients with AIDS. Clin Infect Dis 1999;29:346-51.
14. Rao JS, O'Meara A, Harvey T, Breatnach F. A new approach to the management of Broviac catheter infection. J Hosp Infect 1992;22:109-16.
15. Benezra D, Kiehn TE, Gold JWM, Brown AE, Turnbull ADM, Armstrong D. Prospective study of infections in indwelling central venous catheters using quantitative blood cultures. Am J Med 1988;85:495-8.
16. Raad II, Bodey GP. Infectious complications of indwelling vascular catheters. Clin Infect Dis 1992;15:197-208.
17. Viale P, Pagani L, Petrosillo N, Signorini L, Colombini P, Macri G, et al. Antibiotic lock-technique for the treatment of catheter-related bloodstream infections. J Chemother 2003;15:152-6.
18. Messing B. Catheter-sepsis during home parenteral nutrition: use of the antibiotic-lock technique. Nutrition 1998;14:466-8.
19. Anthony TU, Rubin LG. Stability of antibiotics used for antibiotic-lock treatment of infections of implantable devices (ports). Antimicrob Agents Chemother 1999;43:2074-6.
20. Messing B, Peitra-Cohen S, Debure A, Beliah M, Bernier JJ. Antibiotic-lock technique: a new approach to optimal therapy for catheter-related sepsis in home-parenteral nutrition patients. JPEN J Parenter Enteral Nutr 1988;12:185-9.
21. Johnson DC, Johnson FL, Goldman S. Preliminary results treating persistent central venous catheter infections with the antibiotic lock technique in pediatric patients. Pediatr Infect Dis J 1994;12:930-1.
22. Krzywda EA, Gotoff RA, Andris DA, Marciniak TF, Edmiston CE, Quebbeman EJ. Antibiotic lock treatment (ALT): impact on catheter salvage and cost savings (abstract J 4). Presented at: 35th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, September 17–20, 1995.
23. Krishnasami Z, Carlton D, Bimbo L, Taylor ME, Balkovetz DF, Baker J, et al. Management of hemodialysis catheter–related bacteremia with an adjunctive antibiotic lock solution. Kidney Int 2002;61:1136-42.
24. Guedón C, Nouvellon M, LaLaude O, Lerebours E. Efficacy of antibiotic-lock technique with teicoplanin in *Staphylococcus epidermidis* catheter–related sepsis during long-term parenteral nutrition. JPEN J Parenter Enteral Nutr 2002;26:109-13.
25. Krzywda EA, Andris DA, Edminston CE, Quebbeman EJ. Treatment of Hickman catheter sepsis using antibiotic lock technique. Infect Control Hosp Epidemiol 1995;16:596-8.
26. Capdevila JA, Segarra A, Planes AM, Ramirez-Arellano M, Pahissa A, Piera L, et al. Successful treatment of haemodialysis catheter–related sepsis without catheter removal. Nephrol Dial Transplant 1993;8:231-4.
27. Marr KA, Sexton DJ, Conlon PJ, Corey GR, Schwab SJ, Kirkland KB. Catheter-related bacteremia and outcome of attempted catheter salvage in patients undergoing hemodialysis. Ann Intern Med 1997;127:275-80.
28. Messing B, Man F, Colimon R, Thuillier F, Beliah M. Antibiotic-lock technique is an effective treatment of bacterial catheter-related sepsis during parenteral nutrition. Clin Nutr 1990;9:220-5.
29. Benoit JL, Carandang G, Sitrin M, Arnow PM. Intraluminal antibiotic treatment of central venous catheter infections in patients receiving parenteral nutrition at home. Clin Infect Dis 1995;21:1286-8.
30. Boorgu R, Dubrow AJ, Levin NW, My H, Canaud BJ, Lentino JR, et al. Adjunctive antibiotic/anticoagulant lock therapy in the treatment of bacteremia associated with the use of a subcutaneously implanted hemodialysis access device. ASAIO J 2000;46:767-70.
31. Longuet P, Doudard MC, Arlet G, Molina JM, Benoit C, Leport C. Venous access port-related bacteremia in patients with acquired immunodeficiency syndrome or cancer: the reservoir as a diagnostic and therapeutic tool. Clin Infect Dis 2001;32:1776-83.
32. Arnow PM, Kushner R. *Malassezia furfur* catheter infection cured with antibiotic lock technique. Am J Med 1991;90:128-30.
33. Capdevila JA, Barbera J, Gavalda J, Gasser I, Planes AM, Ocaña I, et al. Diagnosis and conservative management (CM) of infection related to long term venous catheterization (CI) in AIDS patients (abstract J 55). Presented at: 34th Interscience Conference on Antimicrobial Agents and Chemotherapy, Orlando, FL, October 4–7, 1994.
34. Capdevila JA, Segarra A, Planes AM, Gasser I, Gavalda J, Pahissa A. Long term follow-up of patients with catheter related sepsis (CRS) treated without catheter removal (abstract J 3). Presented at: 35th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, September 17–20, 1995.
35. Doudard MC, Arlet G, Leverger G, Paulien R, Waintrop C, Clementi E, et al. Quantitative blood cultures for diagnosis and management of catheter-related sepsis in pediatric hematology and oncology patients. Intensive Care Med 1991;17:30-5.
36. Williams N, Carlson GL, Scott NA, Irving MH. Incidence and management of catheter-related sepsis in patients receiving home parenteral nutrition. Br J Surg 1994;81:392-4.
37. Bregenzer T, Widmer AF. Bloodstream infection from a Port-A-Cath: successful treatment with the antibiotic lock technique (letter). Infect Control Hosp Epidemiol 1996;17:772.
38. Abraham T, Saad N, Balmir E, Pujol F, Scotto M. Treatment of colonized dialysis catheter using antibiotic lock technique (abstract P 455D). Presented at: American Society of Health-System Pharmacists Midyear Clinical Meeting, New Orleans, LA, December 7–11, 2003.
39. Schwarz C, Henrickson KJ, Roghmann K, Powell K. Prevention of bacteremia attributed to luminal colonization of tunneled central venous catheters with vancomycin-susceptible organisms. J Clin Oncol 1990;8:1591-7.
40. Henrickson KJ, Axtell RA, Hoover SM, Kuhn SM, Pritchett J, Kehl SC, et al. Prevention of central venous catheter–related infections and thrombotic events in immunocompromised children by the use of vancomycin/ciprofloxacin/heparin flush solution: a randomized, multicenter, double-blind trial. J Clin Oncol 2000;18:1269-78.
41. Carratalá J, Niubó J, Fernández-Sevilla A, Juvé E, Castellsagué X, Berlanga J, et al. Randomized, double-blind trial of an antibiotic-lock technique for prevention of gram-positive central venous catheter–related infection in neutropenic patients with cancer. Antimicrob Agents Chemother 1999;43:2200-4.
42. Raad I, Darouiche R, Dupuis J, Abid-Said D, Gabrielli A, Hachem R, et al. Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections: a randomized, double-blind trial. Ann Intern Med 1997;127:267-74.
43. Capdevila JA, Gavaldà J, Fortea J, López P, Martin MT, Gomis X, et al. Lack of antimicrobial activity of sodium heparin for treating experimental catheter-related infection due to *Staphylococcus aureus* using the antibiotic-lock technique. Clin Microbiol Infect 2001;7:206-12.
44. Droste JC, Jeraj HA, MacDonald A, Farrington K. Stability and in vitro efficacy of antibiotic-lock solutions potentially useful for treatment of central venous catheter–related sepsis. J Antimicrob Chemother 2003;51:849-55.
45. Haimi-Cohen Y, Husain N, Meenan J, Karayalcin G, Lehrer M, Rubin LG. Vancomycin and ceftazidime bioactivities persist for at least 2 weeks in the lumen of ports: simplifying treatment of port-associated bloodstream infections by using the antibiotic lock technique. Antimicrob Agents Chemother 2001;45:1565-7.
46. Vercaigne LM, Sitar DS, Penner SB, Bernstein K, Burczynski FJ. Antibiotic–heparin lock: in vitro antibiotic stability combined with heparin in a central venous catheter. Pharmacotherapy 2000;20:394-9.
47. Vercaigne LM, Zelenitsky SA, Findlay I, Bernstein K, Penner SB. An in vitro evaluation of the antibiotic/heparin lock to sterilize central venous haemodialysis catheters. J Antimicrob Chemother 2002;49:693-6.
48. Raad I. Management of intravascular catheter–related infections. J Antimicrob Chemother 2000;45:267-70.
49. Kentos A, Struelens MJ, Thys JP. Antibiotic-lock technique for the treatment of central venous catheter infections (letter). Clin Infect Dis 1996;23:418-9.

EXTRACTO

OBJETIVO: Resumir la literatura existente sobre la técnica de utilizar antibióticos en la válvula de los catéteres como una alternativa de tratamiento para pacientes con catéteres altamente necesarios. Se consideran altamente necesarios los catéteres que no pueden o deben ser removidos por la falta de accesos venosos necesarios para la administración endovenosa de terapias tales como nutrición parenteral, diálisis, o quimioterapia.

FUENTES DE INFORMACIÓN: Se utilizo el sistema de MEDLINE e *International Pharmaceutical Abstracts* (1980–agosto 2004). Los términos utilizados para la búsqueda fueron cerradura con antibióticos, infección de catéter, y tratamiento tópico.

SELECCIÓN DE ESTUDIOS/EXTRACCIÓN DE DATA: Se incluyeron estudios en humanos que describían el uso de antibióticos en la válvula de los catéteres como alternativa de tratamiento para infecciones de catéter y estudios que evaluaran la estabilidad in vitro de los antibióticos.

SÍNTESIS: La técnica de utilizar antibióticos en la válvula de los catéteres ha sido utilizada en pacientes con catéteres altamente necesarios, usualmente para la administración de nutrición parenteral, quimioterapia, o diálisis. La tasa porcentual de éxito en preservar el catéter infectado ha sido variable y puede depender del microorganismo asociado a la infección. Además, existe información conflictiva en términos de la compatibilidad de antibióticos con soluciones de heparina.

CONCLUSIONES: El consenso aparenta ser que el uso de antibióticos en la válvula de los catéteres puede ser utilizado en pacientes con catéteres altamente necesarios cuando se documenta una infección por estafilococos coagulasa negativa y no hay signos sistémicos evidentes de sepsis tales como hipotensión. La mayoría de estos pacientes necesitan además terapia sistémica. Una infección de catéter asociada a una bacteremia causada por microorganismos gram negativos o una fungemia probablemente requerirá la remoción del catéter para prevenir complicaciones sistémicas. Se requieren estudios adicionales sobre el uso de antibióticos en la válvula de los catéteres para poder contestar las interrogantes que existen.

Annette Perez

RÉSUMÉ

OBJECTIF: Revoir la littérature médicale concernant l'utilisation de la technique de cathéter à demeure avec antibiotique comme option de traitement pour les patients qui ont un besoin essentiel en cathéters fonctionnels. Les cathéters sont considérés comme besoin hautement nécessaire lorsque leur retrait est impossible ou non désiré en l'absence de sites d'injection alternatifs pour des thérapies tels que l'alimentation parentérale, la dialyse, ou une chimiothérapie anticancéreuse.

SOURCE DE DONNÉES: MEDLINE et résumés pharmaceutiques internationaux (1980 à août 2004). Les termes de recherche incluaient cathéter à demeure avec antibiotique, infection du cathéter, et traitement topique.

SÉLECTION DES ÉTUDES/EXTRACTION DES DONNÉES: Les articles décrivant l'utilisation de la technique du cathéter à demeure avec antibiotique dans le traitement d'infections du cathéter chez les humains et les études évaluant la stabilité in-vitro des antibiotiques ont été inclus.

SYNTHESE DES DONNÉES: La technique du cathéter à demeure avec antibiotique a été utilisée chez les patients avec des besoins hautement nécessaires en cathéters fonctionnels, généralement pour l'alimentation parentérale, la chimiothérapie anticancéreuse, ou la dialyse. Les taux de succès dans la sauvegarde du cathéter infecté sont variables et dépendent du microorganisme infectieux impliqué. De plus, des données conflictuelles existent en ce qui à trait aux compatibilités des antibiotiques avec les solutions d'héparine.

CONCLUSIONS: Un consensus semble être établi à l'effet que la technique de cathéter à demeure avec antibiotique peut être tentée pour les patients avec besoin hautement nécessaire en cathéter lorsqu'une infection à staphylocoques à coagulase négative est documentée et qu'aucun signe systémique de sepsie, tel que l'hypotension, n'est évident. La majorité de ces patients ont probablement besoin également d'une thérapie systémique. Une infection du cathéter associée à une bactériémie gram-négative ou une septicémie à champignons nécessitera probablement le retrait du cathéter afin de prévenir les complications systémiques. Des études additionnelles avec la technique du cathéter à demeure avec antibiotique sont justifiées face aux questions laissées sans réponse.

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