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Editorial

Antibiotic Lock Therapy: Paradism of saving lives and antibiotics

Intravascular catheters have become essential tools for the adequate management of patients in modern medical practice[1]. They are used for the administration of intravenous fluids, medications, blood products, and parenteral nutrition fluids, to provide hemodialysis, and to monitor the hemodynamic status of patients. However, use of central venous catheters (CVCs) can lead to bloodstream infection, frequently referred to as catheter-related bloodstream infection (CRBSI) or catheter-associated bloodstream infection (CABSI). Such infections are associated with serious morbidity and mortality among patients receiving chemotherapy, parenteral nutrition, and hemodialysisand with increased health care costs[2].

Central venous catheter use has increased substantially, and associated infections have become a frequent complication of catheter use. The incidence of catheter-related infections reported in the literature varies from 9% to 80%, depending on catheter type and patient risk factors and on the definition of CRBSI or CABSI that is used.There are several denominators for detection of CRBSI rate, eg. CRBSI rate in 100 CVCs or in 1000 CVC days or in 100 patients. The most recommended denominator of detection of CRBSI rate is the 1000 CVC days[3].

An estimated 250,000 central catheter-related bloodstream infections CRBSI occurred annually in the United States. Several studies revealed that the CRBSI rate is also high in Bangladesh. Infection rates are dependent on the type of CVC used and are reported as the number of bloodstream infections per 1000 intravascular device days[3,6]. CRBSI was diagnosed in 11% and CVC colonization in 43% patients. Rate of CRBSI was 8/1000 CVC days and 11/1000 CVC days in Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital (DMCH), Bangladesh respectively whereas CVC colonization rate was 32/1000 CVC days and 47.5/1000 CVC days in BSMMU and DMCH[4]. Another study conducted in Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Shahbagh, Dhaka, Bangladesh, CRBSI rate was found 16/1000 CVC days and CVC colonization was 48.3/1000 CVC days[5].

The management of catheter-related infection involves decisions regarding the necessity of the removal of the catheter and the administration of antibiotics. The determination of whether the catheter should be removed or remain in place should take into consideration at least three factors: the type of catheter, the type and microbiology of the infection, and the status of the patient[7]. Thus, for peripheral catheters prompt removal remains the mainstay of therapy. On the other hand, although catheter removal is frequently viewed as the only appropriate treatment, this procedure raises important practical problems in 'highly needed' catheters, such as Broviac-Hickman-type catheters and totally implantable venous access devices (ports). These catheters are expensive and they must be implanted and withdrawn in the operating theater. Moreover, these devices are used in patients who are frequently debilitated and with no other available vascular access, such as patients receiving long-term parenteral nutrition, patients requiring dialysis[8,9]. In these clinical settings, an attempt to treat catheter-related bacteremia is often carried out with a seven to 21-day course of systemic antibiotics administered through the catheter without catheter removal. However, this approach fails in approximately 30% of treatments, resulting in removal of the device[10,11].

These failures can be explained, at least partially, by the inability of most antibiotics to kill bacteria growing in a biofilm in therapeutically achievable concentrations. In fact, it is well known that many micro-organisms in the presence of biomaterial will adhere tenaciously to its inert surface[12]. Moreover, several studies have demonstrated that once a micro-organism adheres to the surface of a catheter, its antimicrobial susceptibility is altered and it becomes resistant, or at least tolerant. In addition, biofilm bacteria are also resistant to host defense agents such as phagocytes and antibodies. Importantly, recent investigations have shown that antibiotic concentrations must be 100-1000 times greater to kill biofilm bacteria than to kill bacteria in solution[13].

To overcome these problems, and taking into consideration the fact that the majority of infections in tunnelled catheters originated in the catheter hub and spread intralumenally, an antibiotic-lock technique has been developed for treatment of catheter-related infection. The antibiotic-lock technique consists of filling the catheter lumen with an antibiotic solution and allowing it to dwell for a period of time, in order to sterilize the device[14]. With this method, a high local concentration of an appropriate antibiotic can be applied in the catheter lumen while avoiding systemic toxicity and the need to monitor serum drug levels[15].

In addition, since the catheter is closed, there is no risk of distant spread of micro-organisms, as may occur with continuous perfusion of antibiotics through the infected catheter. The antibiotic-lock technique is particularly appealing for treatment of noncomplicated (absence of hypotension or organ hypoperfusion, septic thrombosis and septic emboli) central venous catheter-related infection of intralumenal origin[16].

Results of several open studies, mainly involving patients receiving home parenteral nutrition, indicate that this method may be regarded as an alternative to the conservative treatment of noncomplicated intraluminal catheter-related bacteremia, in which infection may be treated without catheter removal. However, many questions about this therapeutic method remain to be resolved, including appropriate concentration of antibiotics, duration of treatment, and whether or not concomitant systemic antibiotic therapy is necessary. Prospective studies comparing the antibiotic-lock technique with conventional treatment are needed.

Intraluminal colonization and infection of central venous catheters (CVCs) are associated with the development of microbial biofilm on catheter surfaces. Bacteria in a biofilm can be difficult to eradicate with traditional systemic antibiotic administration and can lead to recurrent CRBSIs[17]. Antibiotic lock therapy (ALT) involves instillation of a highly concentrated antibiotic solution into an intravascular catheter lumen for the purpose of sterilization in order to treat catheter-related bloodstream infections (CRBSIs), minimize associated complications, and avoid catheter removal.Antibiotic concentrations must be 100- to 1000-fold greater to kill sessile bacteria within a biofilm as compared with planktonic bacteria[18].

The antibiotic lock is a highly concentrated antibiotic solution, often combined with an anticoagulant such as heparin, administered in an amount sufficient to fill and dwell in the catheter lumen when the catheter is not in use. Anticoagulants are thought to be beneficial in ALT for treatment of CRBSI by interfering with fibrin formation and allowing increased antibiotic penetration into microbial biofilm. Dwell times may range from four hours to three days, depending on solution stability and amount of time available when the catheter is not in use. Antibiotic lock solutions should be withdrawn from the catheter when it is needed for intravenous access to avoid systemic exposure to high concentrations of antibiotics and/or anticoagulants that can result in toxic effects, particularly with prolonged use or when used in low-weight neonates[19].

Antibiotic lock therapy (ALT) for the prevention and treatment of catheter-related bloodstream infections is a simple strategy in theory, yet its real-world application may be delayed or avoided due to technical questions and/or logistical challenges.

There are a number of potential and documented risks associated with ALT. As with any solution allowed to dwell in a catheter lumen, the potential for occlusion exists. This risk is expected to be decreased if the solution also contains an anticoagulant. Flushing of the lock solution may expose the patient to unnecessary systemic concentrations of antibiotics and/or anticoagulants a risk that increases with flushing frequency. Although some systemic exposure from CVC leakage may be expected, the risk of toxicity is likely quite limited if the lock is aspirated as directed. However, high-concentration antibiotic solutions associated with serious toxicities, eg, aminoglycosides and ototoxicity, should still be avoided. The greatest risk of flushing is likely in lock solutions containing higher concentrations of anticoagulants, particularly heparin >1,000 units/mL or citrate 30%-46.7%. At these concentrations, the patient may be exposed to systemically active doses that would increase risk of bleeding or hypocalcemia and arrhythmias, respectively. Low-level exposure of antibiotics may potentially increase the risk of resistance. However, this concern should be weighed against findings that routine prophylactic use of ALT may reduce the general rate of CRBSI, thereby decreasing overall need for systemic antibiotic therapy.

Given the integral role of long-term CVC use in health care delivery, ALT remains an important option for the preventive and adjunctive treatment of CRBSI. A wide variety of antibiotics have been evaluated for clinical use, with the largest body of data available for vancomycin and gentamicin. In order to ensure optimal clinical outcomes with ALT, clinicians should consider common technical questions and logistical challenges in advance. These include lock preparation procedures, use of additives (eg, heparin, citrate, or EDTA), timing of initiation and therapy duration, dwell time and catheter accessibility, and risks associated with ALT. Development of local protocols is recommended in order to assist clinicians with these potential issues and facilitate utilization of ALT where appropriate.

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