THE EFFICACY OF ALCOHOL-ANTIBIOTIC LOCK THERAPY FOR TREATMENT OF CATHETER RELATED BLOODSTREAM INFECTIONS IN PATIENTS RECEIVING HOME PARENTERAL NUTRITION

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In patients with chronic gastrointestinal tract failure, requiring access to the venous system, the subsequent catheter re-insertion are leading to large veins thrombosis impeding or preventing the insertion of another catheter and exposing patients to the risk of complications. Understanding the pathophysiology of catheter-related infections, enabled to use methods allowing to eradicate the source of infection without removal and replacement of central catheter with a new one. In our center, for many years we have been using an alternative method involving implementation of the alcohol-antibiotic lock in the treatment of infections. This method is based on the assumption that the destruction of biofilm with concentrated alcohol will enable antibiotic penetration and killing other microorganisms. Treatment with alcohol-antibiotic lock lasts from 8 to 10 days and involves filling the catheter with 96% alcohol followed by a solution of the antibiotic of high concentration.

The aim of the study was to evaluate the efficacy of treatment of catheter-related bloodstream infections with two methods (catheter replacement with a new one and the alcohol-antibiotic lock therapy) in patients receiving home parenteral nutrition (HPN).

Material and methods. 428 HPN in the period from 1 January 2005 to 31 December 2010. Among which 240 (56%) of women with an average age of 56.5±16 years and 188 (44%) of men with an average age of 54±17 years. The indications to HPN were as follows: short bowel syndrome in 298 (70%) patients, multilevel obstruction of the gastrointestinal tract in 52 (12%), postoperative gastrointestinal fistulas in 48 (11.2%), malabsorption syndrome in 17 (4%), motility disorders in 6, cachexia in 4 and radiation enteritis in 3 patients.

Results. In 247 (57.5%) from 428 patients, no episode of catheter-related bloodstream infection was found, while 181 were diagnosed with 352 episodes of catheter-related bloodstream infections. In 40 (9.4%) from 428 patients, 168 (47.8%) episodes have been found – almost a half. The mean duration of treatment of patients receiving home parenteral nutrition, starting from the first episode of catheter-related bloodstream infection, in 48 patients treated with the lock was equal to 1053±748 days, and in 133 patients treated with catheter replacement was equal to 952±709 days (t-test p = 0.62).

Conclusions. The survival time of patients treated with alcohol-antibiotic lock is the same as in patients treated with the catheter removal and insertion of the new one. The use of alcohol-antibiotic lock to treat catheter-related bloodstream infections in order to eradicate selected microorganisms that colonize the lumen and cause an infection, is as effective as catheter replacement with a new one.

Key words: home parenteral nutrition, alcohol-antibiotic lock therapy, catheter related bloodstream infections

One of the conditions of success during long-term parenteral nutrition therapy is to avoid complications related to access to the venous system. Despite several methods reducing the risk of colonization and infection that have been developed, including trainings of patient
or caregiver operating catheter, infections still occur. The classic method of catheter related bloodstream infection treatment involves the removal of the catheter, which is the source of infection and appropriate antibiotic administration (1). After taking control over the infection, new catheter is inserted. In order to reduce the risk of infection, a number of measures have been developed to improve the safety of venous line service, which include among the others, new types of plugs, “antibacterial” catheters, new types of dressings and filling catheter when not in use with an antibiotic or other agent of biocidal action, usually ethanol and recently taurolidine. The fundamental treatment method of catheter related bloodstream infections is to remove the catheter – source and at the same time foreign body sustaining infection – and appropriate antibiotic treatment (2). Systemically administered antibiotics kill microorganisms in blood but do not destroy those inhabiting the catheter and infection symptoms recur in 20 to 50%, since the low concentration of the antibiotic in the solution administered intravenously by colonized catheter, does not allow its penetration into the biofilm, which ultimately leads to the removal of the central catheter (3).

In patients still requiring continued access to the venous system, each subsequent catheterization is more difficult and with higher risk of early complications and because of „difficult catheterization” also late complications as thrombosis which makes access to the venous system impossible (4). Ethyl alcohol is antibacterial and fungicidal antiseptic, acting by denaturing the protein and therefore the risk of development of resistance is low. Prolonged exposure of polyurethane and silicone catheters to 96% ethanol did not change their structure and their mechanical properties (5). Filling catheter with ethyl alcohol was used for years in order to clear catheters clogged with lipid-calcium complexes or was administered prophylactically before heparin solution to reduce the risk of colonization, founding the longer use of the catheter (6).

The aim of the study was to evaluate the efficacy of catheter related bloodstream infections treatment in patients receiving long-term home parenteral nutrition and comparison of the two approaches.

### MATERIAL AND METHODS

428 patients, 240 (56%) women aged 16 to 92 years (with average age 56.5±16 years) and 188 (44%) men aged 13 to 96 (with average age 54±17) years. The indications for parenteral nutrition were as follows: short bowel syndrome in 298 patients (70%), multilevel gastrointestinal obstruction impossible for surgical treatment in 52 (12%) patients, postoperative gastrointestinal fistulas in 48 patients (11.2%), malabsorption syndrome in 17 (4%) patients and gastrointestinal motility disorders in 6, cachexia in 4 and radiation enteritis in 3 patients. Among 428 treated patients, connection and disconnection of nutritional mixtures infusion was performed in 239 (55.8%) patients by their caregivers, and 189 (44.2%) patients performed these activities on their own. Broviac catheter was used by 297 (69.4%) patients, Groshong catheter by 60 (14%) patients and Redo TPN catheter by 27 (6.3%) patients.

**Execution of alcohol-antibiotic lock**

![Fig. 1. The course of treatment with alcohol-antibiotic lock](image-url)

* vancomycin – 50mg/ml
  teicoplanin – 40 mg/ml
  amikacin – 100 mg/ml

** volume = internal volume of the catheter

**Statistical analysis**

Comparison of average time of using a new catheter after replacement and catheter treated by alcohol-antibiotic lock was made with Student’s t-test. Time to recurrence of infection depending on the method of treatment was compared using the Kaplan-Meier method, with the assessment of the significance of the obtained results using the Cox-Mantel test. In order to identify the impact of factors associated with infection recurring, multiple regression analysis of factors potentially significant in the univariate analysis was...
performed. IBM SPSS Statistics software (version 21.0) was utilized.

RESULTS

The average time of use of the catheter after an episode of catheter related bloodstream infection, depending on the treatment, to the next episode (infection, death of the patient, end of treatment or observation period) was as follows: after treatment with alcohol-antibiotic lock 436±436 days and after exchange of the catheter 468±441 days (t-test, p = 0.29) (Cox-Mantel test score p = 0.57302 – the difference is not statistically significant) – fig. 2.

Figure 3 shows the recurrence of catheter related bloodstream infections. Time to subsequent infection after infection with gram positive bacteria was an average of 479±465 days, gram-negative bacteria 418±403 days, and for fungal infection 368±254 days (t-test 0.87 and 0.54).

Figure 4 presents the median time of catheter use until infection recurrence, depending on the type of catheter: for the Broviac 333 days, for the Groshong catheter – 286 days and for Redo TPN catheter 281 days.

Average time of Broviac catheter use until the next infection after treatment with alcohol-antibiotic lock was an average of 431±437 and after replacing the catheter with a new one was an average of 465±443 days (t-test p = 0.54). No statistically significant differences were found (Cox-Mantel test score p = 0.40123) with respect to the use of Broviac catheter after an episode of catheter related bloodstream infection until the next infection depending on the method of dealing with the catheter: treatment using antibiotics lock or catheter replacement with a new one – fig. 5.

Probability of patient survival depending on the number of catheter related bloodstream infections in the observation period. The analysis excluded patients with cancer. No significantly longer survival among patients without catheter related infections was found. Survival analysis using a Cox-Mantel test showed a significant difference between the group of patients with no infections in comparison with patients with single infection (p = 0.026). The analysis of survival differences in groups of patients with more catheter related bloodstream infections was not statistically significant – fig. 6.

Cumulative probability of survival without catheter related bloodstream infections during
the observation period in comparison with the group of patients who have five or more infection recurrence in observation. The analysis excluded patients with cancer. No significantly longer survival among patients without catheter related infections was found. Analysis of the survival difference using the Mantel-Cox test $p = 0.19$ – fig. 7.

**DISCUSSION**

Despite advances in diagnosis and treatment of catheter related bloodstream infections in patients requiring long-term vascular access, including patients receiving home parenteral nutrition, catheter related bloodstream infections still remain a serious problem. Among the unresolved issues experts cite a number of specific problems encountered every day by doctors and nurses treating catheter related infections (7). These include:

- the treatment of patients with positive central blood culture and negative peripheral blood culture;
- duration of treatment with antibiotics if catheter was not removed;
- routine control of cultures after treatment;
- proceedings while the outcome of blood culture pending;
- handling with catheters with colonization without bacteremia or fungemia;
- duration of the alcohol-antibiotic lock therapy when antibiotic is administered systemically through the catheter;

- desirability of performing transesophageal echocardiography after infection with Staphylococcus aureus.

Some of these issues are explaining the reported results. Thus, in patients with catheter related bloodstream infections, systemic antibiotic therapy should be applied for at least a week, as in the case of positive central blood cultures with a negative peripheral blood culture and when patient interview indicates the occurrence of the infection. Moreover, it seems that it is advisable to use empiric therapy in each case of suspected catheter related bloodstream infection, because such behavior is associated with a lower risk of infection recurrence. Method of treatment of catheter related infections without removing the catheter, involves a try of sterilizing the inner surface of the catheter with antibiotic or other biocide. For this pur-
pose, the catheter is filled with a solution of a substance having a biocidal effect and closed for a few to 24 hours (8). Hence the word „lock” meaning “close” or “fastener”, which in this case corresponds to the Polish word “plomba”. Bernard Messing, the author of the method, locked catheter filled with an antibiotic, most commonly with amikacin for 12 hours a day and over the next 12 he administrated the mixture for parenteral nutrition, yielding efficiency at a level from 85 to 93%. The duration of treatment ranged from 7 to 20 days, and in patients with good tolerance, treatment was continued at home.

Messing applied systemic antibiotic treatment for 3 days or not at all, not finding a difference in the results (9). Interest in the new method of catheter related infection treatment without catheter removal is high, particularly in relation to patients with chronic dialysis catheters and children and adults receiving long-term parenteral nutrition, although six years ago such method was considered a controversial treatment. Subsequent authors confirmed the effectiveness of the method without removing the catheter in patients receiving home parenteral nutrition at 50 – 92% (10).

In 19 cases, Fortun et al., filled catheter with vancomycin or gentamicin solution at a concentration of 2 mg/ml for 12 hours a day and at the same time systemically administrated antibiotics, the control group consisted of 29 patients treated with intravenously administrated antibiotic. 18 catheter infections were cured, in 2 cases there was a recurrence of the infection. Treatment success was achieved in 84% of patients and in the control group only in 65% of patients, who were treated with only systemically administrated antibiotic (11).

In another prospective randomized study of 46 patients with catheter related bacteremia (40 ports and 6 tunneled catheters), a comparison of the results of treatment with antibiotic lock with placebo for 7-14 days was made. A solution of antibiotic contained vancomycin or ceftazidime in a concentration of 0.5 mg/ml and 100 U/ml of heparin. Treatment success was defined as the behavior of the catheter within an observation period up to 180 days. Satisfactory results were achieved in 67% of patients treated with the lock and in 43% of patients treated with the classically administered antibiotic. In total, infection recurrence was observed in 3 patients treated with antibiotic lock and in 9 patients receiving placebo (12). In the evaluation of treatment results of 115 episodes of catheter related bacteremia treated with antibiotic lock with a concentration of 2 mg/ml of vancomycin, ciprofloxacin or amikacin, the cure, defined as negative blood culture in one month after the end of treatment, was achieved in 82% of cases. The failure predominantly, because in 45% of cases, was reported in the case of Staphylococcus aureus infections (13). In the case of hospital acquired infections where treatment with antibiotic lock was initiated immediately after suspicion of infection arose, the success was achieved in 93.3% of cases and in half of these cases reduction of systemic antibiotics treatment to 48 hours was made (14). In the case of coagulase-negative staphylococcal infections with increased resistance to vancomycin, linezolid in antibiotic lock was applied to children (15). In the most cases, the antibiotic at a concentration from 2 to 5 mg/ml was applied; there were also published studies in which teicoplanin at a concentration of 10 mg/ml or higher was used or amikacin at a concentration of 10 mg/ml with heparin solution. One of the problems is the emergence of antibiotic resistance, but it has never been described as a result of the use of antibiotic lock. It seems that the used alcohol-antibiotic lock is an effective and safe alternative to a traditional catheter replacement with intravenous antibiotics therapy.

**CONCLUSIONS**

1. Survival of patients treated with alcohol-antibiotic lock is the same as of patients treated with the removal and insertion of a new catheter.
2. The use of alcohol-antibiotic lock to treat catheter related bloodstream infections for the eradication of selected microorganisms colonizing the lumen of the catheter and causing this infection is as effective as catheter replacement with a new one.
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