New Treatment for Percutaneous Sites in Patients with a Ventricular Assist Device: Nihon University Crystal Violet Method

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Background: Infection of the percutaneous site of a ventricular assist device (VAD) is a challenging complication. We report our experience with crystal violet Solbase (Nihon University crystal violet method) for prevention of driveline or cannula infections in VAD patients.

Patients and Methods: The crystal violet method was used in 10 patients (prophylaxis in nine and treatment in one). Eight patients had an extracorporeal VAD (Nipro) and two had an implantable VAD (Heart Mate II).

Results: The infection-free period was 4–623 days (mean: 144.2 ± 222.9 days). All eight patients with an extracorporeal VAD died, while the two patients with an implantable VAD (Heart Mate II) survived. Infection was improved in a patient with MRSA, and the results of bacteriological examination were always negative in the patients receiving prophylaxis. The two patients with an implantable VAD had no infection for 2 and 20 months after implantation.

Conclusion: These findings suggest that the Nihon University crystal violet method is effective for prevention and treatment of driveline or cannula infections in patients with a VAD.

Keywords: infection, ventricular assist device, crystal violet

Introduction

Development of smaller continuous flow ventricular assist devices (VADs) has dramatically improved the long-term outcome compared with earlier devices and has made long-term use feasible.1–4) Cerebrovascular disorders and percutaneous site (cannula site and driveline) infections are the most frequent complications after VAD implantation. It has been reported that VAD-related infections occur in 9.8%–51.9% of patients at an average of 68 days to 9.2 months after implantation and can have a major influence on survival.5–9) Although the incidence of infection decreased following the introduction of continuous flow VADs compared with pulsatile flow VADs,8) infectious complications are increasing again due to long-term VAD use for destination therapy and other purposes.9) However, a widely accepted regimen for preventing percutaneous site infection after VAD implantation has not been established, with different methods of disinfection being employed at various centers.

Methylrosanilinium chloride (Pyoktanin, gentian violet, or crystal violet) is a triphenylmethane pigment that was synthesized in the 1860s, and is well known as a blue pigment employed for gram staining as well as an antimicrobial/antiparasitic agent.10) Methylrosanilinium chloride is cheap, shows antimicrobial activity against gram-positive bacteria and Pseudomonas aeruginosa, and is listed among the WHO Essential Medicines as a safe antimicrobial agent. After long neglect, methylrosanilinium chloride has recently been
rediscovered and is currently used to treat prosthetic graft infection\textsuperscript{11,12} and decubitus ulcer\textsuperscript{13} due to its potent antibacterial activity against methicillin-resistant Staphylococcus aureus (MRSA). However, a liquid formulation has been used in most studies to date. We previously prepared an ointment by adding methylrosanilinium chloride to Solbase and used it successfully to treat MRSA infection at the cannula site in patients with an extracorporeal VAD.\textsuperscript{14} Since then, we have been using this ointment for prevention of percutaneous site infection and we review the results obtained here.

Patients and Methods

The subjects were eight men and two women aged 25–64 years (mean age: 47.5 ± 11.3 years). The VAD was implanted because of acute myocardial infarction in three patients, ventricular septal perforation secondary to acute myocardial infarction in one patient, dilated cardiomyopathy in three patients, fulminant myocarditis in two patients, and ischemic cardiomyopathy in one patient.

Topical application of methylrosanilinium chloride ointment (Nihon University crystal violet method) to the percutaneous site was performed in all 10 patients for prevention (n = 9) or treatment (n = 1) of infection. One patient with an extracorporeal VAD (Nipro) was treated for MRSA infection of the percutaneous site, while the ointment was used for prophylaxis of infection in seven patients with an extracorporeal VAD and two patients with an implantable VAD (HeartMate II). The ointment was applied to the percutaneous site once daily in the patient with MRSA infection and was applied once daily after surgery in the patients receiving prophylaxis (Fig. 1).

Regarding antibiotic therapy, the patient with MRSA infection received vancomycin, while the other nine patients received piperacillin and cefazolin from just before surgery until removal of the drain tube. For disinfection of the percutaneous site, an ethanol swab was used up to postoperative day 3, after which chlorhexidine was employed. Following disinfection, the cannula or driveline site was covered with crystal violet Solbase (0.01% methylrosanilinium chloride in Solbase [macrogol 400:50 g and macrogol 4000:50 g]) (Fig. 2). For the patients with HeartMate II, a doctor performed disinfection for the first 2 weeks, after which the patients performed disinfection themselves using cotton swabs soaked in benzalkonium chloride and then covered the percutaneous site with crystal violet Solbase. During hospitalization, weekly testing of the percutaneous site for bacterial infection was conducted.

Results

The patient with an implantable HeartMate II could be weaned from the VAD, but the eight patients with extracorporeal devices all died (due to multiple organ failure in four patients, cerebral infarction in two patients, cerebral hemorrhage in one patient, and right heart failure in one patient).

The infection-free period achieved with use of the ointment was 4–623 days (mean: 144.2 ± 222.9 days). Although all of the patients with an extracorporeal VAD died, infection was improved in the patient with MRSA infection of the percutaneous site and bacteriological tests were consistently negative in the patients receiving prophylaxis. The patients with a HeartMate II VAD did not develop infection for 2 and 20 months after implantation (Table 1). Results of weekly bacterial tests of the cannula or driveline site during hospitalization were negative in all patients receiving preventive disinfection. Both white blood cell (WBC) and C-reactive protein (CRP) increased after surgery to reach a peak on postoperative day 3 and then declined (Fig. 3).
Discussion

It has been reported that the antimicrobial activity of methylrosanilinium chloride is not reduced by the presence of serum or exudate, so efficacy for exudative wounds can be expected unlike povidone iodine. It has also been reported that cutaneous/mucous membrane disorders caused by methylrosanilinium chloride are mainly due to a primary concentration-dependent irritant effect, while a lower concentration does not affect epithelial regeneration.\textsuperscript{15-17} Due to its potent antibacterial activity against MRSA, methylrosanilinium chloride has increasingly been used for the treatment of prosthetic graft infection\textsuperscript{11,12} and decubitus ulcer\textsuperscript{13} over the past several years. However, liquid preparations of methylrosanilinium chloride were used in previous studies and a method of percutaneous site disinfection for VAD patients has not been established. Liquid methylrosanilinium chloride is used for percutaneous site infections at some centers in Japan, but there is no published literature and its efficacy has not been documented. We combined methylrosanilinium chloride with Solbase to prepare an ointment. Solbase (Macrogol
ointment) is a water-soluble ointment base which is poorly absorbed through the skin, but promotes the percutaneous absorption of other agents. It is effective for accelerating the healing of skin or mucosal wounds and preventing bacterial invasion by protecting the wound, absorbing secretions, accelerating drying, and promoting granulation. Because it is water-soluble, Solbase can be easily washed off and does not prevent observation of the wound.

Various methods for the prevention and treatment of percutaneous site infection in VAD patients have been reported. At the University of Pittsburgh, driveline infection was improved by application of honey. It has been reported that the high level of sugar in honey reduces intracellular water and inhibits infection, while gluconic acid in honey has an antimicrobial effect. Platelet-rich plasma and allogeneic platelet gel were also reported to be effective for driveline infections. This method requires centrifugation of a patient’s blood to obtain concentrated platelets for application to the percutaneous site. The growth factors in platelets are expected to accelerate tissue regeneration and repair, but efficacy has not been demonstrated because only a case report has been published and the method has not been studied in a sufficient number of patients.

Limitations

The number of patients studied was small and about half of them died within 2 weeks of the initiation of disinfection. Accordingly, further long-term follow-up is needed to confirm the antibacterial activity of crystal violet Solbase. We plan to accumulate more patients and follow them for an extended period in order to clarify the efficacy of this ointment.

Disclosure Statement

Akira Sezai has received lecture fees from Daiichi Sankyo Company. The other authors have no conflicts of interest associated with this study.

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