



Successful Treatment for Methicillin Resistant *Staphylococcus aureus* Conjunctivitis Using 1% Povidone Iodine Eye Drop: Two Cases

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Authors' contributions

This work was carried out in collaboration between all authors. Author KM, YT and RU was the treating clinician in this case. Authors KM and YI wrote the protocol. Author KM and YT managed the literature searches and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Purpose: Long-term bedridden patients frequently present with refractory chronic conjunctivitis. Multidrug-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), are often isolated; infections caused by such bacteria are treated with vancomycin, although refraining from overuse of this drug is recommended. Bacterial resistance to povidone-iodine (PI) has not been observed; hence, it can be effectively used for treating bacterial infections. However, it has not been popularly used for treating ocular surface infections. We report two cases of multidrug-resistant bacterial conjunctivitis treated with PI.

Methods: Case 1: A 90-year-old male hospitalized for pneumonia caused by multidrug-resistant *Pseudomonas aeruginosa*. Case 2: A 56-year-old male hospitalized for brainstem hemorrhage. In both patients, there were signs of conjunctivitis and MRSA was cultured. To avoid overuse of vancomycin, we started 1% PI instillation thrice daily.

Results: Clinical signs of the patients remarkably improved within a week of PI treatment. There were no distinct complications from PI treatment in either case.

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Conclusions: PI has a wide spectrum, does not induce bacterial resistance, is cheap, and can be obtained worldwide. Though further studies are necessary for wider practical use in clinical settings, PI ocular instillation is a reasonable option for treating ocular surface infections caused by multidrug-resistant bacteria, which are overseen by many general ophthalmologists.

Keywords: Povidone iodine; Methicillin resistant Staphylococcus aureus; conjunctivitis.

ABBREVIATIONS

PI: Povidone-iodine
 MRSA: Methicillin-resistant *Staphylococcus aureus*

of PI treatment and were resolved in 2 weeks as determined by a negative culture.

Table 1. Antibiotic susceptibilities for isolated bacteria

	Case 1		Case 2
	MRSA	MRCNS	MRSA
Cefmenoxime	R	R	R
Ceftazidime	R	R	R
Cefozopran	R	R	R
Cefdinir	R	R	R
Flomoxef	R	R	R
Imipenem	R	S	R
Gentamicin	R	R	R
Amikacin	R	S	R
Erythromycin	R	S	R
Vancomycin	S	S	S
Levofloxacin	R	R	R
Moxifloxacin	R	R	R
Gatifloxacin	R	R	R
Clarithromycin	R	S	R
Minocycline	R	S	R
Chloramphenicol	R	R	S

1. CASE PRESENTATION

Long-term bedridden patients are usually immunocompromised and present with contaminated eyelid margins, reduced blinking, and dysfunction of tears, leading to refractory chronic conjunctivitis [1]. Multiple prescriptions of antibacterial eye drops may be ineffective. Multidrug-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), are often isolated; infections caused by such bacteria are treated with vancomycin [2], although refraining from overuse of this drug is recommended because of the possible emergence of vancomycin-resistant strains.

Povidone-iodine (PI) is commonly used for perioperative disinfection. Bacterial resistance to PI has not been observed; hence, it can be effectively used for treating bacterial infections. However, PI has not been popular for treating ocular surface infections, with only few reports on its use [3-6]. We report two cases of multidrug-resistant bacterial conjunctivitis treated with PI.

1.1 Case 1

A 90-year-old male was hospitalized for pneumonia caused by multidrug-resistant *Pseudomonas aeruginosa* at the Nojima Hospital in October 2016, and he was given intravenous antibiotics (ceftriaxone and sultamicillin). The patient was bedridden and was unable to have a conversation. In January 2017, the patient was referred to the Department of Ophthalmology for bilateral eye discharge. Levofloxacin eye drops were used four times a day for 2 weeks, but his symptoms did not improve. Multidrug-resistant MRSA was detected (Table 1), which was resistant to all antibacterial drugs except vancomycin. To avoid overuse of vancomycin, we started 1% PI instillation thrice daily. His clinical signs remarkably improved after 1 week

1.2 Case 2

A 56-year-old male was hospitalized for brainstem hemorrhage at the Nojima Hospital in May 2015. The patient was unable to move except for movements like blinking and moving his fingertips. He had multiple episodes of fever in June, September, and December of 2015. MRSA was cultured from sputum, and antibiotics (isepamicin, ceftazidime, imipenem, minocycline, teicoplanin, and cefazolin) were administered systemically. Subsequently, he had multiple episodes of fever, and intravenous administration of antibiotics was repeated. He was unable to completely close his left eyelid, and therefore, ofloxacin ointment was continuously applied to prevent exposure keratitis. In December 2015, redness and discharge were noted in his left eye, and MRSA was cultured from conjunctiva. These symptoms were reduced with chloramphenicol instillation in a week. In February 2017, conjunctivitis recurred, and MRSA was cultured again (Table 1). We started 1% PI instillation thrice daily. Ofloxacin ointment was continued to

prevent drying of the ocular surface. His clinical signs remarkably improved within a week of PI treatment, but slight redness and corneal epithelial disorder remained because of incomplete eyelid closure. After confirming the negative culture twice at 1 and 2 weeks following the initiation of PI treatment, PI was discontinued.

During the course of treatment, the corneal epithelium of both the patients was observed under fluorescein staining, and there were no distinct complications from PI treatment in either case.

In the present study, 1% PI was employed. 5 ml of 10% povidone iodine was diluted with 45 ml of saline, and divided into the sterilized 5 ml dropper.

Written informed consent for publication was obtained from patient's family.

3. DISCUSSION

It was indicated that PI can be used to treat ocular surface infections [3]. Schuhman et al. used PI for treating 40 cases of conjunctivitis and confirmed that 38 of the 40 subjects had healed and the remaining two showed improvement over a period of 6 days [4]. PI was used for treating 459 cases of infectious conjunctivitis in children and demonstrated effects equal to antibacterial agents [5].

Similar effects of PI can be expected against multidrug-resistant bacteria. Taylor et al. reported a case of refractory chronic conjunctivitis caused by MRSA in a patient with giant fornix syndrome, which was effectively treated with PI [6]. However, they had used a combination of triamcinolone and vancomycin, which makes it difficult to make a judgment on the effects of PI alone.

Case 1 was successfully treated with PI alone. Although Case 2 continued to use an antibacterial ointment to prevent drying of the ocular surface (which started before the use of PI), the improvement in the signs of conjunctivitis was thought to be because of the use of PI.

Short-term use of highly concentrated antibacterial agents, such as eye drops, is less likely to induce resistance. However, long-term or repeated use of antibiotic eye drops has been reported to cause resistance [7,8]. Long-term bedridden patients may suffer from recurrent conjunctivitis, resulting in prolonged or repeated

vancomycin administration. PI ocular instillation can prevent the occurrence of resistant strains; therefore, it should be more commonly used to prevent the overuse of vancomycin.

There are some problems with PI treatment. First, high-concentration PI ocular instillation causes irritation to the ocular surface [9]. In a report that compared 1.25% and 5% PI for preoperative disinfection prior to an intravitreal injection of therapeutic agents, the effects were equivalent. However, approximately 6% of patients complained of irritation with 5% PI, whereas there were no complaints of irritation with 1.25% PI [10]. Isenberg et al. mentioned that the concentration was changed from 2.5% (original) to 1.25% because mild stinging was noted with the former [5]. These reports indicate that PI eye drops (1%–1.25%) are effective and well-tolerated agents for the treatment of non-specific ocular surface infections.

Second, PI is not suitable for long-term storage because the active free iodine in PI becomes inactive over time. If it is completely sealed, it can be stored for a long time. However, it is unknown how long an effective concentration can be maintained because air enters the container every time it is opened several times a day in cases of eye instillation. Therefore, even if iodine was still remaining in the bottle, we replaced it with a new bottle once a week. For practical use, the concentration must be selected to minimize irritation while maintaining a concentration that works effectively. It would be ideal to prepare PI in small sealed containers for individual use.

4. CONCLUSIONS

PI ocular instillation has a wide spectrum of antibacterial activity, does not induce bacterial resistance, is cheap, and can be obtained worldwide. Though further studies are necessary for wider practical use, PI ocular instillation is a reasonable option for treating ocular surface infections caused by multidrug-resistant bacteria.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

All authors hereby declare that all the treatment have been examined and approved by ethic

committee of Nojima hospital and have been performed in accordance with the ethical standards laid in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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