

Successful treatment for Methicillin-resistant staphylococcus aureus conjunctivitis using

1% Povidone iodine eyedrop: two cases.

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: Case1: A 90-year-old male hospitalized for pneumonia caused by multidrug-resistant *Pseudomonas aeruginosa*. Case2: 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

20 treatment. There were no distinct complications from PI treatment in either case.

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

26

27 **Keywords**

28 Povidone iodine; Methicillin-resistant staphylococcus aureus; conjunctivitis

29

30 **Abbreviations**

31 PI: Povidone-iodine

32 MRSA: methicillin-resistant *Staphylococcus aureus*

33 **Text**

34 Long-term bedridden patients are usually immunocompromised and present with contaminated
35 eyelid margins, reduced blinking, and dysfunction of tears, leading to refractory chronic
36 conjunctivitis¹. Multiple prescriptions of antibacterial eyedrops may be ineffective.
37 Multidrug-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA),
38 are often isolated; infections caused by such bacteria are treated with vancomycin², although

39 refraining from overuse of this drug is recommended because of the possible emergence of
40 vancomycin-resistant strains.

41 Povidone-iodine (PI) is commonly used for periorerative disinfection. Bacterial resistance to
42 PI has not been observed;hence, it can be effectively used for treating bacterial
43 infections.However, PI has not been popularl for treating ocular surface infections, with only
44 few reports on its use³⁻⁶. We report two cases of multidrug-resistant bacterial conjunctivitis
45 treated with PI.

46

47 **Case1**

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

58

59 **Case2**

60 A 56-year-old male was hospitalized for brainstem hemorrhage at the Nojima Hospital in May
61 2015. The patient was unable to move except for movements like blinking and moving his
62 fingertips. He had multiple episodes of fever in June, September, and December of 2015.
63 MRSA was cultured from sputum, and antibiotics (seipamicin, ceftazidime, imipenem,
64 minocycline, teicoplanin, and cefazolin) were administered systemically. Subsequently, he
65 had multiple episodes of fever, and intravenous administration of antibiotics was repeated. He
66 was unable to completely close his left eyelid, and therefore, ofloxacin ointment was
67 continuously applied to prevent exposure keratitis. In December 2015, redness and discharge
68 were noted in his left eye, and MRSA was cultured from conjunctiva. These symptoms were
69 reduced with chloramphenicol instillation in a week. In February 2017, conjunctivitis recurred,
70 and MRSA was cultured again (Table 1). We started 1% PI instillation thrice daily. Ofloxacin
71 ointment was continued to prevent drying of the ocular surface. His clinical signs remarkably
72 improved within a week of PI treatment, but slight redness and corneal epithelial disorder
73 remained because of incomplete eyelid closure. After confirming the negative culture twice at
74 1 and 2 weeks following the initiation of PI treatment, PI was discontinued.

75

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

78

79 In the present study, 1% PI was employed. 5ml of 10% povidone iodine was diluted with
80 45ml of saline, and divided into the sterilized 5ml dropper.

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

82

83 **Discussion**

84 It was indicated that PI can be used to treat ocular surface infections³. Schuhman et al. used PI
85 for treating 40 cases of conjunctivitis and confirmed that 38 of the 40 subjects had healed and
86 the remaining two showed improvement over a period of 6 days⁴. PI was used for treating
87 459 cases of infectious conjunctivitis in children and demonstrated effects equal to
88 antibacterial agents⁵.

89

90 Similar effects of PI can be expected against multidrug-resistant bacteria. Taylor et al. reported
91 a case of refractory chronic conjunctivitis caused by MRSA in a patient with giant fornix
92 syndrome, which was effectively treated with PI⁶. However, they had used a combination of
93 triamcinolone and vancomycin, which makes it difficult to make a judgment on the effects of
94 PI alone.

95

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

100 Short-term use of highly concentrated antibacterial agents, such as eye drops, is less likely to
101 induce resistance. However, long-term or repeated use of antibiotic eyedrops has been
102 reported to cause resistance^{7,8}. Long-term bedridden patients may suffer from recurrent
103 conjunctivitis, resulting in prolonged or repeated vancomycin administration. PI ocular
104 instillation can prevent the occurrence of resistant strains; therefore, it should be more
105 commonly used to prevent the overuse of vancomycin.

106

107 There are some problems with PI treatment. First, high-concentration PI ocular instillation
108 causes irritation to the ocular surface⁹. In a report that compared 1.25% and 5% PI for
109 preoperative disinfection prior to an intravitreal injection of therapeutic agents, the effects
110 were equivalent. However, approximately 6% of patients complained of irritation with 5% PI,
111 whereas there were no complaints of irritation with 1.25% PI¹⁰. Isenberg et al. mentioned that
112 the concentration was changed from 2.5% (original) to 1.25% because mild stinging was
113 noted with the former⁵. These reports indicate that PI eye drops (1%–1.25%) are effective and
114 well-tolerated agents for the treatment of non-specific ocular surface infections.

115

116 Second, PI is not suitable for long-term storage because the active free iodine in PI
117 becomes inactive over time. If it is completely sealed, it can be stored for a long time.

118 However, it is unknown how long an effective concentration can be maintained because air
119 enters the container every time it is opened several times a day in cases of eye instillation.
120 Therefore, even if iodine was still remaining in the bottle, we replaced it with a new bottle
121 once a week. For practical use, the concentration must be selected to minimize irritation
122 while maintaining a concentration that works effectively. It would be ideal to prepare PI in
123 small sealed containers for individual use.

124

125 **Conclusions**

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

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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
Flomox	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
Minomycin	R	S	R
Chloramphenicol	R	R	S
