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Heiman F.L. Wertheim
Medical Microbiology
L348
Erasmus MC
Dr Molewaterplein 40
3015 GD Rotterdam

Tel: 0104633510
Fax:
E-mail: h.wertheim@erasmusmc.nl

Budget: **2230**

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Heiman F.L. Wertheim Erasmus MC
Medical Microbiology
Dr Molewaterplein 40
3015 GD Rotterdam

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Clinical trial

Topical gentian violet for cutaneous infection and nasal carriage with MRSA

Masaki Okano, MD, Sanai Noguchi, MD, Koshi Tabata, MD, and Yasutaka Matsumoto, MD

From the Departments of Dermatology and Internal Medicine, and Sections of Medical Technology and Pharmaceuticals, Aizenbashi Hospital, Osaka, Japan

Correspondence
Masaki Okano, MD
Department of Dermatology
Aizenbashi Hospital
Higashi 3-1-11
Nippombashi
Naniwa-ku
Osaka 556-0006
Japan

This study describes a potential effect of topical gentian violet on cutaneous infection and nasal carriage with methicillin-resistant *Staphylococcus aureus* (MRSA). 0.5% gentian violet was used in 28 cases of skin lesions once a day, while a 0.3% solution was applied on the nasal vestibules of nine cases twice a day. The period for eradication in the 28 skin cases was 9.1 ± 6.0 days. It was 15.3 ± 9.0 days for the nine nasal lesions. The minimal inhibitory concentration (MIC) of gentian violet against MRSA from the four isolated strains was 0.0225 ± 0.0096 μg/mL. No adverse reactions occurred throughout the study. It is suggested that gentian violet may be potentially effective against MRSA.

We prospectively studied 37 randomized cases of cutaneous infection or nasal carriage with methicillin-resistant *Staphylococcus aureus* (MRSA) (16 boys and men and 21 girls and women; ages varied from 0 to 91 years; mean, 35.3 ± 33.1 years) in order to evaluate the clinical and bacteriologic effectiveness of topical gentian violet.

Materials and methods

Gentian violet (Ishizu Seiyaku Ltd, Osaka, Japan) was prepared as an aqueous solution. Gentian violet solution was used at a concentration of 0.5% once a day in 28 cases of skin lesions, while a 0.3% solution was applied by scrubbing on the anterior nares twice a day in nine cases of nasal lesions. No other topical or systemic antimicrobial was allowed during the study.

Clinical specimens were collected using swabs from skin or nasal lesions before and after gentian violet treatment, until MRSA was not isolated at all. MRSA was incubated on an MRSA screening agar (Becton Dickinson and Company, MD, USA), and was detected by the method of the National Committee for Clinical Laboratory Standards (NCCLS).[1] The criterion for inclusion was one positive culture. The definition of disinfection depended on both clinical healing and eradication of MRSA for cutaneous infection. Only eradication was necessary for nasal carriage.

The minimal inhibitory concentration (MIC) was determined using the broth macrodilution methods recommended by the NCCLS.[2] Briefly, the microorganisms from four MRSA strains were grown finally at 100,000 colony forming units (cfu)/mL in Mueller-Hinton II broth medium (Becton Dickinson and Company, MD, USA) to which gentian violet was added to a final concentration of 50 to 0.001 μg/mL. The MIC was defined as the lowest concentration that inhibited growth completely. The MICs were recorded after 24 h of incubation at 35 °C.

Data were expressed as the mean ± SD. Significance was estimated with Student's *t*-test.

Results

Table 1 summarizes the clinical and bacteriologic effectiveness of topical gentian violet on MRSA. Underlying diseases of nasal MRSA carriers included pulmonary tumor, Ménière's disease, cerebral infarction, allergic

Table 1 Clinical and bacteriologic effectiveness of topical gentian violet on MRSA

Disease	Number	Age Mean ± SD (Range)	Days for eradication Mean ± SD (Range)
Infectious erosion	12	38.2 ± 31.7 0–83	6.9 ± 3.9 2–14
Impetigo	8	14.6 ± 24.8 1–71	6.8 ± 3.7 4–15
Umbilical infection	2	0.0 ± 0.0 0–0	11.5 ± 6.4 7–16
Infectious ulcer	3	78.0 ± 17.6 58–91	16.3 ± 11.1 6–28
Decubitus ulcer	1	76.0 ± 0.0	12.0 ± 0.0
Angular cheilitis	1	71.0 ± 0.0	16.0 ± 0.0
Paronychia	1	4.0 ± 0.0	19.0 ± 0.0
Subtotal	28	34.3 ± 34.1 0–91	9.1 ± 6.0 2–28
Nasal carriage	9	38.6 ± 31.4 1–87	15.3 ± 9.0 4–28
Total	37	35.3 ± 33.1 0–91	10.6 ± 7.2 2–28

rhinitis, atopic dermatitis, prurigo, herpes simplex, and impetigo.

Disinfection of MRSA with this bactericide required a period from 2 to 28 days (mean, 10.6 ± 7.2 days) for all cases. The time to eradication in the 28 skin cases ranged from 2 to 28 days (mean, 9.1 ± 6.0 days). The time to eradication varied from 4 to 28 days (mean, 15.3 ± 9.0 days) for the nine nasal cases.

No adverse reactions occurred, except for purple color staining of the skin throughout the study.

The MICs of gentian violet against MRSA from the four isolated strains were 0.01, 0.02, 0.03, and 0.03 μg/mL, respectively (mean, 0.0225 ± 0.0096 μg/mL).

Discussion

The development and spread of multiple antimicrobial-resistant *Staphylococcus aureus* have gained worldwide attention over the years. Vancomycin is currently the antimicrobial of choice for systemic infection induced by MRSA. Resistance to vancomycin would be extremely worrying.[3] Haley *et al.*[4] reported that povidone-iodine was the most rapidly bactericidal agent *in vitro* against MRSA of the commonly used antiseptics, such as hexachlorophene, chlorhexidine gluconate, *p*-chloro-*m*-xylenol, and povidone-iodine. Povidone-iodine is, however, rapidly neutralized in the presence of organic materials such as blood or sputum.[2] In fact, its clinical effect is often disappointing on exudatively excoriative or ulcerative skin lesions infected with MRSA.

Recent laboratory data have suggested that gentian violet may be efficient against MRSA.[5] In addition, eradication of MRSA from decubitus ulcers with gentian violet has been reported.[6]

According to previous data,[5] the MIC of gentian violet against MRSA from four strains was between 1.6 and 6.3 μg/mL (mean, 3.2 ± 2.2 μg/mL), whereas that of povidone-iodine was 5000 μg/mL. The minimal bactericidal concentration (MBC) of gentian violet against MRSA from the same strains was between 25 and 200 μg/mL (mean, 131.3 ± 85.1 μg/mL), and the MBC was not influenced even when the culture medium contained 25% human whole serum, while that of povidone-iodine against MRSA was 10,000 μg/mL.

In the present study, topical gentian violet achieved disinfection of MRSA in a period ranging from 2 to 28 days (mean, 10.6 ± 7.2 days) for all cases. Nasal disinfection tended to require a longer period (mean, 15.3 ± 9.0 days) than the eradication of MRSA in cutaneous lesions (mean, 9.1 ± 6.0 days). We did not undertake a follow-up study to ensure that long-term eradication had been acquired. The *in vitro* susceptibility test of gentian violet against MRSA disclosed a mean MIC value of 0.0225 μg/mL, which was approximately 140-fold of that presented by Saji.[5] The considerable difference between the two MIC values was assumed to be due to a disparity in the bacterial density of the final dilutions for culture.

The use of gentian violet in the treatment of superficial skin infections was suggested as early as 1912 by Churchman.[7] Gentian violet is a triphenylmethane rosaniline dye, and is bacteriostatic and bactericidal to Gram-positive bacteria, including streptococci and staphylococci, and to many fungi.[8–11] Hypersensitivity to gentian violet has been rarely reported.[12] The susceptibility of Gram-positive bacteria to the rosaniline dyes is presumably associated with the characteristics of the cell that underlie the differential Gram stain. Furthermore, we assume that the clinical potency of this antiseptic is related to its properties as a dye, which enable it to permeate and stain the tissue, and consequently to maintain an antimicrobial action there for a longer time.

The clinical virtue of this antiseptic against MRSA has seldom been referred to. The present investigation has confirmed the clinical efficacy of topical gentian violet against MRSA, reported by Saji *et al.*[6] in several kinds of skin lesions infected with MRSA, and clarified that the dye is possibly effective in nasal MRSA carriage. This is, to our knowledge, the first report in the English literature of a trial use of this disinfectant against nasal carriage of MRSA.

The prevalence of MRSA is a social problem. Nosocomial infections caused by this bacterium result in significant morbidity and cost to hospitalized patients.

Gentian violet is inexpensive and the techniques for its application are simple. It is suggested that, in spite of its conspicuous color, topical gentian violet may be useful and potentially effective against MRSA.

Further comparative studies are needed.

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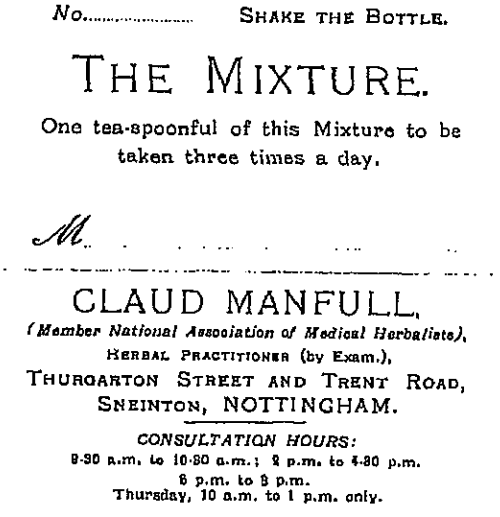

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