



Appropriate Treatment using Povidone-Iodine for Atopic Dermatitis

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Abstract

We have proposed a combination therapy using a disinfectant as a countermeasure against *Staphylococcus aureus*, which is often detected on the skin, in the treatment of moisturizer ointment and steroid ointment, which are common for the treatment of atopic dermatitis. During treatment, many cases experienced improvement in skin rash and dramatic improvement in laboratory data. The treatment method that combines this general treatment method with disinfection therapy was named Staphylococcal disinfection skin care method [1]. (In Japan, this treatment is called Isodine® therapy [2].)

By the way, Yamada et al. [3] reported a complication of colitis in patients with atopic dermatitis. Kira et al. [4] reported a complication of myelitis in patients with atopic dermatitis. Therefore, we also performed duodenal biopsy, neurology examination, and cervical spine MRI for many patients with atopic dermatitis. As a result, many cases of atopic dermatitis showed damage to the cervical spine and duodenum. In addition, we experienced many cases in which these disorders were observed at the same time in the same case [5,6,7]. Therefore, we estimated the involvement of the toxin (which is called superantigen [8,9]) produced by *S. aureus* not only in the skin but also in the intestinal tract and cervical spine, and concluded that atopic dermatitis is a superantigen disease [10]. Therefore, considering the importance of treatment against toxins that cause damage not only to the skin but also to multiple organs, we would like you to practice this treatment method that we have developed from the early stages of treatment for patients with atopic dermatitis.

CLINICAL BACKGROUND IN PATIENTS WITH ATOPIC DERMATITIS

1. Skin culture results

In the skin culture of 607 patients with mild to severe atopic dermatitis who first visited our hospital in 1995, methicillin-sensitive *S. aureus* was isolated in 55.0%, coagulase-negative staphylococci in 17.5%, both methicillin-sensitive *S. aureus* and coagulase-negative staphylococci in 17.5% and methicillin-resistant *S. aureus* in 1.6%. No growth was found in only 8.4% [1].

The frequency of MRSA examined in the same manner was 4.2% in 109 cases in 2003, which increased in a few years compared to 1.6% in 1995 [1-7].

2. Toxin produced by *Staphylococcus aureus*

S. aureus produces many toxins. The toxin was measured using the PCR method, and the toxins included staphylococcal enterotoxin A (B, C, E), toxic shock syndrome toxin 1 and exfoliative toxin A (B).

The total detection rate of toxins was 80.1% from 196 *S. aureus* strains [7].

Currently, clinical antitoxin IgE antibody measurements are available for Staphylococcal Enterotoxin A (SEA) and SEB. The total rate for SEA and SEB detection was 60.2% [7].

As you can see in the **Table 1**, we have already reported the results of toxins produced by 196 strains of *S. aureus*.

The detection rates of staphylococcal enterotoxins A, B, C and E were 9.7, 55.6, 7.7 and 30.6%, respectively. The detection rate of toxic shock syndrome toxin 1 was 6.6% and those of exfoliative toxins A and B were 4.1 and 1.5% [7]. The positive rate of toxin was as high as 80.1% from 196 strains of *S. aureus* detected in atopic dermatitis [8-10].

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Table 1. Toxins detected by PCR from *S. aureus* obtained from skin lesions (n = 196).

Detection rate, %	
Total	80.1 (157/196)
SEA	9.7
SEB	55.6
SEC	7.7
SEE	30.6
TSST-1	6.6
ETA	4.1
ETB	1.5
Toxins found in lesions, n	
SEA	7
SEB	59
SEC	2
SEE	16
SEA, SEB	9
SEA, SEE	1
SEA, TSST-1	1
SEA, SEB, SEE	1
SEB, SEC, SEE	3
SEB, SEC, SEE, TSST-1	1
SEB, SEC, TSST-1	1
SEB, SEE	33
SEB, SEC, ETA	1
SEC, SEE	2
TSST-1 only	5
TSST-1, SEC	5
ETA	6
SEE, ETA	1
SEE, ETB	1
SEB, ETB	1
SEE, ETB	1
None	39 39/196 about 20%
Total	196

SEs= staphylococcal enterotoxins (A,B,C,E); TSST-1=Toxic Shock Syndrome Toxin 1; ETA, ETB=Exfoliative toxin A,B Toxins such as SEs, TSST-1 and ETA/B were detected from as many as 80.1% of the strains. When SEA and SEB are combined, the detection rate was 60.2%.

3. Organ disorders other than skin disorders in atopic dermatitis

Regarding the neurological abnormalities [11] sometimes seen in patients with atopic dermatitis, we confirmed the neurological abnormalities in 89 out of 110 patients (80.9%) with atopic dermatitis. MRI was also used to observe cervical spine abnormalities in 54 of 69 atopic dermatitis patients (78.2%) who showed neurological abnormalities. Twenty-

one of 32 atopic dermatitis patients (65.6%) were observed for both duodenal and cervical spine injuries [10] (Table 2).

Table 2. Duodenal biopsy and Cervical MRI findings and Clinical diagnosis.

Case	Age	Histological diagnosis	MRI diagnosis	Clinical diagnosis
1	43	Chronic Duodenitis	CS, OYL	CM
2	32	Chronic Duodenitis	CS	CM
3	31	Chronic Duodenitis	CS	CM
4	26	Chronic Duodenitis	WNR	CM
5	21	Chronic Duodenitis	WNR	CM
6	23	Chronic Duodenitis		WNR
7	25	Chronic Duodenitis	CS	CM
8	28	Mild Duodenitis	CS	CM
9	24	Chronic Duodenitis	WNR	CM
10	36	Chronic Duodenitis	CS	CM
11	33	Duodenitis	WNR	CM
12	24	Mild Duodenitis	CS	CM
13	29	Chronic Duodenitis	CS	CM
14	28	Duodenitis	CS	CM
15	26	Duodenitis	WNR	WNR
16	24	Mild Duodenitis	CS	CM
17	28	Mild Duodenitis	CS	CM
18	20	Chronic Duodenitis		WNR
19	25	Chronic Duodenitis	CS	CM
20	21	Chronic Duodenitis	CS	CM
21	32	WNR	CS	CM
22	28	WNR	CS	CM
23	24	Chronic Duodenitis	CS	CM
24	26	Chronic Duodenitis	CS	CM
25	28	WNR	CS	CM
26	30	Chronic Duodenitis	CS	CM
27	34	WNR	CS	CM
28	21	Chronic Duodenitis	CS	CM
29	38	WNR	CS	CM
30	30	Chronic Duodenitis		WNR
31	34	Slight Duodenitis		WNR
32	32	Mild Duodenitis		WNR

In addition, duodenal inflammation was observed in 43 of 53 patients with atopic dermatitis duodenal biopsy. Of the 12 patients who had repeated duodenal biopsies, 5 of the 12 patients who had repeated duodenal biopsies normalized duodenal inflammation and the rash with the staphylococcal disinfectant skin care method we developed for atopic dermatitis [10].

4. Clinical experience with this treatment

We have already reported in several papers that in many cases this treatment improves total IgE levels and antitoxin IgE antibody levels against Staphylococcal Enterotoxin A (SEA) and SEB [12,13] almost in parallel in a short period of time.

We have experienced a dramatic improvement in serum TARC levels in many cases with this treatment. We have already reported one case [14].

The sterilization time of Povidone iodine solution against *S. aureus* is said to be 20 to 30 sec. It is estimated that a considerable number of *S. aureus* remains in the 20 to 30 sec application period of Povidone iodine solution, as opposed to *S. aureus* in places such as the skin surface where organic substances (plasma components, etc.) are present. To support this, Haley CE [15] reported that a considerable number of MRSA bacteria remained even after applying povidone iodine solution to MRSA on the skin for 30 sec to 1 min.

Since the skin on the face is anatomically thin and vulnerable to irritation, we set the Povidone iodine solution on the face for 2 min as a countermeasure against *S. aureus* in patients with atopic dermatitis over 5 years old. And for other bodies, the application time of povidone iodine solution was set to 3 min, and a treatment method was proposed in which the povidone iodine solution was completely rinsed with water after application [1,16,17]. (We wrote in Paper 16 entitled Significance of Disinfectants for the Treatment of Atopic Dermatitis that the sterilization time for *S. aureus* povidone iodine solution is 5 seconds. But that was a mistake and we should have written that the sterilization time is 20-30 seconds. We apologize for correcting the mistake.)

It has already been reported that there is no problem with thyroid disorders by flushing the povidone iodine solution in a short time. For skin with atopic dermatitis under 5 years old, we use a diluted povidone iodine solution. And clinical improvement has been experienced in many cases with this application time. We also applied this treatment to 25 patients with atopic dermatitis in which MRSA was detected on the skin, and already reported that MRSA was able to be eradicated in all cases in a short period of time [2].

DISCUSSION

Atopic dermatitis is a disease whose main lesion is pruritus with repeated exacerbations and remissions, and it is defined that many patients have atopic predisposition. Many factors are involved in exacerbation and remission.

Kobayashi [18] reported that *S. aureus* is involved in the onset and exacerbation of atopic dermatitis.

We thought that the involvement of *S. aureus* is particularly important among the many factors involved in exacerbation and remission. We have developed Isodine® therapy [2], which is a combination of disinfectant therapy and general treatment, as a countermeasure against *S. aureus* in atopic dermatitis. We have experienced a short-term improvement in skin rash with this treatment in many cases. We also

experienced dramatic improvements in laboratory test values in many cases.

The use of povidone iodine solution was described for the first time in atopic dermatitis in Japan's Atopic Dermatitis Clinical Practice Guideline 2018 [19]. In this guideline, there is no medical basis to actively recommend the use of povidone iodine solution. It is difficult to treat with basic treatment such as topical steroids, and it may be considered as an adjunct therapy for cases in which infection is thought to be involved in the cause, but it should not be done easily because of safety concerns.

In addition, since this treatment improves the improvement of many test values of patients with atopic dermatitis in a relatively short period of time, we wondered if the disorder of atopic dermatitis could not be explained only by the skin. Therefore, after seeing reports that atopic dermatitis was a disorder of the intestinal tract and cervical spine, we tried duodenal biopsy and neurological diagnosis and examination. In many cases, not only skin but also multi-organ disorders were observed in the same case. It was presumed that the toxin produced by *S. aureus* detected on the skin of atopic dermatitis affects multi-organ damage [10,16,17].

In addition, although the frequency of MRSA detected on the skin of atopic dermatitis has increased recently, we have already been able to eradicate MRSA in all 25 cases of atopic dermatitis with this treatment method.

In Japan's 2019 Treatment Guidelines for MRSA Infections-Revised Edition [20], MRSA is detected in 10 to 30% of *S. aureus* detected in outpatients. This Isodine® therapy is effective as a countermeasure against MRSA, and it can be eradicated in all cases, so we would like to recommend it as an appropriate treatment for the treatment of atopic dermatitis.

By the way, already in 2003, Dhafer Laouini [21] showed that epicutaneous exposure skews the response to superantigen toward TH2 cells, leading to allergic skin inflammation and increased IgE synthesis, which are characteristic of atopic dermatitis. Furthermore, they suggest that therapies that effectively decrease skin colonization with superantigen-producing organisms might have a beneficial effect in atopic dermatitis.

Therefore, we sincerely hope that the treatment method we have developed will spread from the early stage of treatment for patients with atopic dermatitis as a countermeasure against toxins that cause damage not only to the skin but also to multiple organs.

REFERENCES

- 1 Sugimoto K, Kuroki H, Kanazawa M, Kurosaki T, Abe H, et al. (1997) New successful treatment with disinfectant for atopic dermatitis. *Dermatology* 195: 62-68.
- 2 Sugimoto K, Ishikawa N, Sugioka T (1998) Isojin®

- disinfectant therapy for atopic dermatitis. JPN J Pediatr Dermatol 17: 103-107.
- 3 Yamada H, Izutani R, Chihara J, Yodate T, Matsukura M, et al. (1996) RANTES mRNA expression in skin and colon of patients with atopic dermatitis. Int Arch Allergy Immunol 111: 19-21.
 - 4 Kira J, Yamasaki K, Kawano Y, Kobayashi T (1997) Acute myelitis associated with hyperIgEemia and atopic dermatitis. J Neurol Sci 148: 199-203.
 - 5 Sugimoto K, Ishikawa N, Ogawa A (1998) Treatment of *Staphylococcus aureus* by disinfection treatment of patients with atopic dermatitis. Hifu (The Skin) 40: 117-124.
 - 6 Sugimoto K, Ishikawa N, Sugioka T, Koseki H, Kubosawa H (2002) The importance of disinfection therapy using povidone-iodine solution in atopic dermatitis. Dermatology 204: 63-69.
 - 7 Sugimoto K, Ishikawa N, Terano T, Kitukawa Y, Kubosawa H, et al. (2006) The importance of bacterial superantigens produced by *Staphylococcus aureus* in the treatment of atopic dermatitis using povidone-iodine. Dermatology 212: 26-34.
 - 8 White J, Herman A, Pullen AM, Kubo R, Kappler JW, et al. (1989) The Vbeta-specific superantigen staphylococcal enterotoxin B: Stimulation of mature T cells and clonal detection in neonatal mice. Cell 56: 17-35.
 - 9 Uchiyama T, Yan XJ, Imanishi K, Yagi L (1994) Bacterial superantigens - Mechanisms of T cell activation by the superantigens and their role in the pathogenesis of infectious disease. Microbiol Immunol 38: 245-256.
 - 10 Sugimoto K, Kitukawa Y, Aotsuka A, Wada T, Kubosawa H, et al. (2015) Is Atopic Dermatitis One of the Superantigens Diseases? J Dermatol Clin Res 3: 1052-1053.
 - 11 Ito S, Hattori T, Fukutake T, Sugimoto K (2003) Is atopic dermatitis a risk factor for intervertebral disc degeneration? A preliminary clinical and MRI study. J Neurol Sci 206: 39-42.
 - 12 Skov L, Olsen JV, Giorno R, Schlievert PM, Baadsgaard O, et al. (2000) Application of staphylococcal enterotoxin B on normal and atopic skin induced up-regulation of T cells by a superantigen-mediated mechanism. J Allergy Clin Immunol 105: 820-826.
 - 13 Sugimoto K (2016) *Staphylococcus aureus* vs Atopic Dermatitis. J Pharm Microbiol 2: 1-3.
 - 14 Sugimoto K, Hattori T, Kitukawa Y, Aotsuka A, Wada T, et al. (2018) Significance of Disinfectants for the Treatment of Atopic Dermatitis, J Allergy Ther 9: 1-3
 - 15 Haley CE, Marling-Cason M, Smith JW, Luby JP, Mackowiak PA (1985) Bactericidal activity of antiseptics against methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol 21: 991-992.
 - 16 Sugimoto K, Hattori T, Kitukawa Y, Aotsuka A, Wada T, et al. (2019) Antiseptic Treatment of Povidone-Iodine Solution as a Countermeasure against *Staphylococcus Aureus* in Atopic Dermatitis. Dermatol Res 1(1): 1-3.
 - 17 Sugimoto K, Hattori T, Kitukawa Y, Aotsuka A, Wada T, et al. (2017) Importance of Measures against *Staphylococcus aureus* in Atopic Dermatitis as a Superantigen Disease. Sci J Clin Res Dermatol 2: 7-9.
 - 18 Kobayashi T, Glatz M, Horiuchi K, Kawasaki H, Akiyama H, et al. (2015) *Dysbiosis* and *Staphylococcus aureus* Colonization Drives Inflammation in Atopic Dermatitis. Immunity 42: 756-766.
 - 19 Journal of Japanese Dermatological Association, Atopic Dermatitis Clinical Practice Guideline (2018) Journal of Japanese Dermatological Association. 128(12): 2431-2502.
 - 20 Editing, MRSA Infectious Disease Treatment Guideline Development Committee, MRSA Infectious Disease Treatment Guidelines-Revised-2019, in Japan.
 - 21 Laouini D, Kawamoto S, Yalcindag A, Bryce P, Mizoguchi E, et al. (2003) Epicutaneous sensitization with superantigen induces allergic skin inflammation. J Allergy Clin Immunol 112(5): 981-987.