Received: 6 March 2019 | Accepted: 4 June 2019

DOI: 10.1002/cia2.12069

ORIGINAL ARTICLE

Journal of Cutaneous Immunology and Allergy

WILEY

Twenty cases of allergic contact dermatitis due to benzoyl peroxide in acne patients in Japan

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Abstract

Background: Benzoyl peroxide is a topical antiacne drug, which also acts as a strong irritant and a weak allergen. Only a few acne patients with allergic contact dermatitis due to benzoyl peroxide gel have been diagnosed by patch testing in Japan. Therefore, the number of such patients is probably underestimated.

Objectives: To correctly diagnose such cases by patch testing and to determine their characteristics and frequency.

Patients and methods: Twenty acne patients that were diagnosed with allergic contact dermatitis between April 2015 and April 2018 were enrolled in this study. Patch tests were performed with acne gels containing benzoyl peroxide and 1% benzoyl peroxide in petrolatum. The patients' profiles and the frequency of dermatitis were analyzed.

Results: All of the patients were female, and their mean age was 24.1 ± 9.3 years. Two patients were suffering from atopic dermatitis. The onset of allergic contact dermatitis occurred at 1 to 2 days, 9 to 28 days, and >30 days (longest: up to 24 months) after the initial application of the causative substance in 3 patients, 9 patients, and 8 patients, respectively. The frequency of such cases was 4.5% at our clinic.

Conclusions: Benzoyl peroxide gels for acne were demonstrated to often act as allergic contact allergens, and thus, dermatologists should be aware of their allergenicity and be apprehensive about markedly increasing the use of such gels in the future.

KEYWORDS

acne, allergenicity, allergic contact dermatitis, benzoyl peroxide, Japan

1 | INTRODUCTION

Benzoyl peroxide is a topical antiacne drug, which has been widely used all over the world for about 60 years. At present, many acne patients can freely purchase benzoyl peroxide-containing products as over-the-counter drugs. In Japan, it has been possible for acne gels containing benzoyl peroxide to be prescribed at medical institutions since 2015, which dermatologists had long desired. So far, there are three kinds of acne gels containing benzoyl peroxide available for medical use, which are 2.5% benzoyl peroxide gel (BPO gel) (Bepio®, Maruho Co), 1% clindamycin (CLDM) and 3% benzoyl peroxide combination gel (CLDM/BPO gel) (Duac®, Pola Pharma Co), and 0.1% adapalene and 2.5% benzoyl peroxide combination gel (adapalene/BPO gel) (Epiduo®, Maruho Co). These gels are markedly effective against acne, but adverse effects were detected in 43.7%, 30.6%, and 10.8% of patients, respectively, at the time of the approval of these gels. The most common of these adverse effects were dryness, erythema, desquamation, and a tingling sensation at the application

site, which were considered to be due to irritant contact dermatitis because benzoyl peroxide is a strong irritant, but a weak allergen. However, some cases of allergic contact dermatitis due to benzoyl peroxide have been reported in other countries.[1–3] In Japan, although these gels have only been in medical use for a couple of years, a few cases of allergic contact dermatitis that were diagnosed using patch testing due to benzoyl peroxide have been reported, and the authors concluded that the clinical findings of the allergic and irritant dermatitis induced by these gels were very similar.[4]

In the present study, we reported the cases of 20 acne patients with allergic contact dermatitis due to benzoyl peroxide, who were diagnosed based on patch testing and their clinical histories and findings at our institutions. In addition, we analyzed the characteristics and frequency of such cases.

2 | PATIENTS AND METHODS

We investigated the cases of 24 patients who suffered adverse effects at the application site after using acne gel containing benzoyl peroxide and were forced to stop using the gel between April 2015 and April 2018. Among them, 2 patients were diagnosed with irritant contact dermatitis due to acne gel based on patch tests and their clinical histories. One patient did not exhibit irritation or allergic reactions during patch testing: that is, they displayed negative results, and one refused to undergo patch testing. Thus, 20 patients were enrolled in this study.

In each case, we took a history of the patient's present illness and investigated complications, the acne gel used for treatment, the affected sites, the duration of application, the presence/absence of skin dryness before onset, systemic adverse effects, the treatments employed, and the outcomes. Patch tests were performed in all 20 patients using Finn Chambers® (SmartPractice) on Scanpor® tape (Norgesplaster A/S), which was applied to the outer aspect of the upper arms. Readings were done on day (D) 2, D3, and D7 after the application of the test substance, according to the International Contact Dermatitis Research Group criteria. The patch test materials and allergens used included 1% benzoyl peroxide in petrolatum (Brial Allergen GmbH, Germany; 1% BPO pet.); acne gels containing benzoyl peroxide (BPO gel, CLDM/BPO gel, and adapalene/BPO gel); other acne gels or creams, such as 0.1% adapalene gel (Differin®, Maruho Co); 1% nadifloxacin cream (Acuatim®, Otsuka Pharmaceutical Co); 1% clindamycin gel (Dalacin T®, Sato Pharmaceutical Co); and 5% propylene glycol (Tokyo Chemical Industry Co).

This study was approved by the medical ethical committee in Ryugasaki Saiseikai General Hospital (No. 201901).

3 | RESULTS

Profiles of the 20 patients are listed in Table 1. Their mean age was 24.1 ± 9.3 (11-41) years, and all of them were female. The following complications relating to allergies were encountered: pollinosis in 4 patients, atopic dermatitis and urticaria in 2 patients each, and asthma and oral allergy syndrome in one patient each. Fourteen patients applied BPO gel, 4 patients applied CLDM/BPO gel, one patient applied both BPO gel and CLDM/BPO gel, and one patient applied adapalene/BPO gel. All skin rashes appeared at a gel application site. The onset of allergic contact dermatitis occurred after 1 to 2 days, 9 to 28 days, and >30 days (longest: up to 24 months) after the initial application of the causative substance in 3 patients, 9 patients, and 8 patients, respectively. Six patients felt dryness at the application site just before the onset of dermatitis. One patient (case 10) was complicated with respiratory distress at the onset of dermatitis. All patients except one (case 10) were successfully treated with mild steroid ointments within a week. Thirteen of the 20 patients were prescribed benzoyl peroxide-containing acne gels at Hanamizuki Clinic, and a total of 286 patients were treated with these gels during the same period. Thus, the frequency of allergic contact dermatitis due to benzoyl peroxide was 4.5% (13/286) at our clinic.

The results of the patch testing are shown in Table 2. The results obtained for BPO gel, CLDM/BPO gel, and adapalene/BPO gel were similar, so Table 2 only shows the results for BPO gel and 1% BPO pet. Regarding the patch test results obtained for BPO gel on D3, the results were classified as ++ in 9 patients and + in 11 patients. As for the patch test results obtained for 1% BPO pet. on D3, the results were classified as ++ in 3 patients, + in 14 patients, and +? in 3 patients. No other acne gels or creams produced positive results, nor did 5% propylene glycol.

4 | DISCUSSION

Benzoyl peroxide is typical organic peroxide and is used to treat acne; bleach flour, hair, and textiles; whiten teeth; and as a radical initiator to induce polymerization. Although benzoyl peroxide is recognized as a cause of allergic contact dermatitis due to various products, such as adhesive tape,[5] swimming goggles,[6] dental prostheses,[7] and bone cement,[8] and some industrial substances/clothing,[9,10] benzoyl peroxide sensitization due to the use of topical acne preparations is rarely reported, and so the number of such cases might be underestimated.[11,12] In previous overseas studies that examined allergic contact dermatitis due to benzoyl peroxide among acne patients, the frequency of such cases was reported to be 0% (0/155),[13] 0.2% (1/445),[14] 1% (2/204),[15] and 5.1% (3/59).[16]

In our study, which was conducted in Japan, 4.5% of the patients that were treated for acne developed allergic contact dermatitis due to topical gels containing benzoyl peroxide, which is a comparatively high frequency, suggesting that it is not uncommon. All of the patients with allergic contact dermatitis were female; however, no significant predilection for either sex was detected (chi-square test) because 86.2% of the acne patients at our clinic were female. Furthermore, atopic dermatitis was not found to be associated with allergic contact dermatitis because only 2 of the 20 patients with allergic contact dermatitis had atopic dermatitis. The

TABLE 1 Profile and characteristics of 20 cases of allergic contact dermatitis due to benzoyl peroxide in acne patients in Japan

	Name	Age/sex	Complications	Acne gel used for treatment	Affected sites	Duration of application	Skin dryness before onset	Systemic adverse effects	Treatment for adverse effects	Duration of treatment
1	EM	40F	Hypomenorrhea, depression	BPO gel	Forehead	10 days	-	-	Hydrocortisone butyrate ointment, olopatadine	4 days
2	HE	29F	Anemia, pollinosis	BPO gel	Neck	9 days	+	-	Clobetasone butyrate ointment	a week
3	AY	14F	Cholinergic urticaria	CLDM/BPO gel	Forehead	24 days	-	-	Olopatadine	a week
4	UT	29F	Ulcerative colitis	CLDM/BPO gel	Cheeks, chin	9 days	+	-	Clobetasone butyrate ointment	4 days
5	CY	26F	-	CLDM/BPO gel	Mandible	1 day	-	-	-	3 days
6	MH	23F	Oral allergy syndrome, pollinosis	BPO gel	Forehead, cheeks	19 days	+	-	Clobetasone butyrate ointment, fexofenadine	3 days
7	MI	14F	Atopic dermatitis	BPO gel	Forehead, cheeks	2 months	-	-	-	a week
8	MW	32F	-	BPO gel	Forehead, cheeks, neck	28 days	+	-	Alclometasone dipropionate ointment, fexofenadine	a week
9	MS	24F	-	BPO gel	Forehead, cheeks, chin	2 days	-	-	Clobetasone butyrate ointment, fexofenadine	5 days
10	NI	11F	Chronic urticaria, asthma	BPO gel	Forehead, cheeks	12 days	-	Respiratory distress	200 mg hydrocortisone + 20 ml glycyrrhizinate + 5 mg chlorpheniramine [DIV], 4 mg betamethasone [DIV], 10 mg prednisolone, 2 days	9 days
11	YY	34F	Pollinosis	BPO gel	Around eyes, cheeks	4 months	-	-	Clobetasone butyrate ointment	1 day
12	AS	34F	Pollinosis	BPO gel	Between eyebrows, cheeks, chin	4 months	-	-	Alclometasone dipropionate ointment	2 days
13	MT	11F	-	BPO gel	Forehead, cheeks, chin	11 days	+	-	Alclometasone dipropionate ointment, fexofenadine	3 days
14	JT	18F	-	BPO gel, CLDM/BPO gel	Mandibles, chin	19 months	-	-	-	2 days
15	TN	27F	-	BPO gel	Chin, nose	13 months	-	-	-	1 day
16	MI	41F	-	BPO gel	Mandibles	7 months	-	-	-	1 day
17	CH	18F	-	BPO gel	Cheeks	2 months	-	-	-	3 days
18	MY	25F	Atopic dermatitis	Adapalene/BPO gel	Chin	24 months	+	-	-	3 days

(Continues)

TABLE 1 (Continued)

	Name	Age/sex	Complications	Acne gel used for treatment	Affected sites	Duration of application	Skin dryness before onset	Systemic adverse effects	Treatment for adverse effects	Duration of treatment
19	AN	16F	-	BPO gel	Between eyebrows, cheeks	1 day	-	-	Clobetasone butyrate ointment	2 days
20	SN	15F	-	CLDM/BPO gel	Whole face	15 days	-	-	Alclometasone dipropionate ointment, bilastine	4 days

Abbreviations: adapalene/BPO gel, 0.1% adapalene, and 2.5% benzoyl peroxide gel; BPO gel, 2.5% benzoyl peroxide gel.; CLDM/BPO gel, 1% clindamycin and 3% benzoyl peroxide gel.

TABLE 2 Patch test results for BPO gel and 1% BPO pet

		BPO gel			1%BPO pet.		
	Name	D2	D3	D7	D2	D3	D7
1	EM	++	++	++	++	++	++
2	HE	+	+	++	+?	+	+
3	AY	+	++	++	+	+	+
4	UT	+	+	+	+?	+	+
5	CY	+?	++	+	+?	++	++
6	MH	-	+	+	-	+	+
7	MI	+	++	++	+	+	UD
8	MW	+	++	+	+	+	+?
9	MS	+	++	+	+	+	+
10	NI	++	++	NR	++	++	NR
11	YY	-	+	+	-	+?	+?
12	AS	+	+	+	+?	+?	+?
13	MT	++	++	+	+	+	+
14	JT	+	+	+	+	+	+?
15	TN	-	+	+	-	+	+
16	MI	+	+	+	+?	+	+
17	CH	+	+	+	+	+	+
18	MY	+	+	+	+	+	+
19	AN	+	++	+	+	+?	+
20	SN	+	+	+	+	+	+

Abbreviations: NR, not read; UD, undeterminable because of scratching.

onset of allergic contact dermatitis occurred at various points after the initiation of acne treatment. Patients who had been using acne gel for ≥9 days were assumed to have become sensitized to benzoyl peroxide during their acne treatment. It is worth mentioning that the longest period between the initial application of the acne gel and the occurrence of allergic contact dermatitis was 24 months. Among the 3 patients who developed allergic contact dermatitis within 2 days of their initial use of BPO gel, patients 5 and 9 might have become sensitized to benzoyl peroxide during their previous application of skincare products containing benzoyl peroxide. The remaining patient (patient 19) developed allergic contact dermatitis the day after they first applied the gel. She was considered to have become sensitized to benzoyl peroxide before the current episode; however, she had never previously used skincare products containing benzoyl peroxide, nor had she undergone treatment involving dental or orthopedic prostheses.

In a study involving patch testing of dental materials conducted in Japan in 2003,[17] 1% BPO pet. produced a positivity rate of 2.7% among 334 patients with various types of dermatitis. The highest positivity rate was seen in the contact dermatitis group, and higher positivity rates were detected in male patients than in female patients and in older patients than in younger patients. On the other hand, a study of patch testing of 1% BPO pet. performed in Germany revealed a 7.8% positivity rate among 29 758 patients, and higher frequencies of positivity were seen in females and younger patients.[18]

In the current study, one of the 20 patients suffered respiratory distress when she was still in elementary school. In the emergency room, her vital signs, including her arterial oxygen saturation level, were within normal limits, and no wheezing or general wheals appeared. We assume that the respiratory distress was induced by mental factors, such as anxiety.

We demonstrated that benzoyl peroxide gels for acne frequently induced allergic contact dermatitis, and thus, dermatologists should be aware of their allergenicity when treating acne patients and be apprehensive about markedly increasing the use of such gels in the future.

CONFLICT OF INTEREST

The authors declares no conflict of interest.

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How to cite this article: Iijima S, Tsunoda T. Twenty cases of allergic contact dermatitis due to benzoyl peroxide in acne patients in Japan. *J Cutan Immunol Allergy*. 2019;2:108–112. https://doi.org/10.1002/cia2.12069