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Original Article

Comparison between Patch Test Results using Patch Test Panel® (S) and Japanese Standard Allergen Series (2008)

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Abstract

Patch testing (PT) is useful for identifying the cause of treatment-resistant dermatitis. The Japanese standard allergen series (2008) (JSA2008) is useful for identifying allergens among substances producing false negative PT results and for revealing unexpected causes of allergic reactions. When performing PT, JSA2008 should be used as much as possible. However, since 2015, Patch Test Panel® (S) has also been available in Japan. This is a ready-to-use PT consisting of 22 standard allergens. Given that 21 of the 22 allergens are shared with JSA2008, Patch Test Panel®(S) is now becoming popular because of its ease of use and timesaving advantage. However, a comparison between PT results using Patch Test Panel®(S) and JSA2008 has not been reported in patients living in northern Kyushu. This study compared the PT results using Patch Test Panel®(S) with those using JSA2008 in patients who visited Kyushu University Hospital and Fukuoka Dental College Hospital. Significantly higher rates of positive PT results were found for gold sodium thiosulfate ($p < 0.001$) and nickel sulfate ($p < 0.001$) using Patch Test Panel®(S).

Key words : patch testing, ready-to-use, Patch Test Panel®(S), Japanese standard allergen (2008)

Introduction

Patch testing (PT) is useful for identifying the cause of treatment-resistant dermatitis[1)2)]. Standard PT series comprise the substances that most commonly cause allergic dermatitis in each country. Monitoring the standard series has proven helpful in detecting chronological changes in the pattern and frequency of the responsible allergens[3)]. In general, allergens in the standard series show positive PT reactions at a rate greater than 0.5% to 1.0%[4)], or are those to which patients have frequent exposure[5)]. Allergens are added or deleted depending on current trends in allergenicity[6)], leading to series variation within institutions over time.

The Japanese standard allergen (JSA) series includes allergens in the living enviro nment that frequently induce sensitization in Japan[7)]. The JSA series is useful in screening for causative allergens in intractable contact dermatitis. The JSA series is compatible with the T.R.U.E. test® (Thin-Layer Rapid Use Epicutaneous Patch Test) released in 1987 in Sweden. The JSA series was approved by The Japanese Society for Dermatoallergology and Contact Dermatitis in 1994 and thereafter was revised to JSA2008. JSA2008 has been recommended for use in PT.

Meanwhile, Patch Test Panel® (S) has been available in Japan since 2015[8)]. This is a ready-to-use PT consisting of 22 standard allergens, of which 21 are also included in JSA2008. Because of

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Table 1 Allergens and allergen content in Patch Test Panel®(S)

Allergen	Content (per specimen)	Additive
1. Nickel sulfate	0.16 mg	Hydroxypropyl cellulose
2. Lanolin alcohol	0.81 mg	Povidone
3. Fradiomycin sulfate	0.49 mg	Povidone
4. Potassium dichromate	0.044 mg	Povidone
5. Caine mix	0.51 mg	Povidone
6. Fragrance mix	0.402 mg	Povidone, β-cyclodextrin
7. Rosin	0.97 mg	Povidone, Butylhydroxyanisole, Dibutylhydroxytoluene
8. Paraben mix	0.80 mg	Povidone
9. None		
10. Balsam of Peru	0.65 mg	Povidone
11. Gold sodium thiosulfate	0.061 mg	Hydroxypropyl cellulose
12. Cobalt chloride	0.016 mg	Hydroxypropyl cellulose
13. p-Tert-butylphenol-formaldehyde resin	0.036 mg	Hydroxypropyl cellulose
14. Epoxy resin	0.041 mg	Hydroxypropyl cellulose
15. Carba mix	0.204 mg	Hydroxypropyl cellulose
16. Black rubber mix	0.060 mg	Povidone
17. Isothiazolinone mix	0.0032 mg	Povidone
18. None		
19. Mercaptobenzothiazole	0.061 mg	Povidone
20. Paraphenylenediamine	0.065 mg	Povidone
21. Formaldehyde	0.150 mg	Povidone, Dry sodium carbonate, Sodium hydrogen carbonate
22. Mercapto mix	0.060 mg	Povidone
23. Thimerosal	0.0057 mg	Povidone
24. Thiuram mix	0.022 mg	Povidone

its ease of use and timesaving advantage, Patch Test Panel®(S) is now becoming popular in clinical use. However, a comparison between PT results using Patch Test Panel®(S) and JSA2008 has not been reported in patients living in northern Kyushu. This study compared the rates of positive PT results in 52 cases using Patch Test Panel®(S) with those in 235 cases using JSA2008.

Materials and Methods

Background

All PT data are maintained at Kyushu University and Fukuoka Dental College. The study was approved by the institutional ethics committee. Patch Test Panel® (S) was used in 52 cases between October 2015 and October 2017, and JSA2008 was used in 235 cases between April 2009 and March 2013.

Patch Test Panel®(S) and JSA2008

Allergens and contents of Patch Test Panel®(S) and JSA2008 are shown in Table 1 and 2, respectively. Mercaptobenzothiazole in Patch Test Panel®(S) is not included in JSA2008, while primin, urushiol, sesquiterpene lactone mix, and mercuric chloride in JSA2008 are not included in Patch Test Panel®(S). The allergen concentrations in Patch Test Panel®(S) are labeled as allergen content in hydroxypropyl cellulose membranes.

Methods and Statistical Analysis

Patch Test Panel®(S) and JSA2008 were used for PT on the upper arm or back for 48 hours and test sites were evaluated at 72 and 168 hours after initial placement. Positive reactions were evaluated according to the diagnostic criteria of the

Table 2 Allergens and allergen content in Japanese standard allergen (2008)

Allergen	Concentration/base
1. Cobalt chloride	1% pet.
2. Paraphenylenediamine black rubber mix	0.6% pet.
3. Gold sodium thiosulfate	0.5% pet.
4. Thiuram mix	1.25% pet.
5. Nickel sulfate	2.5% pet.
6. Mercapto mix	2% pet.
7. Dithiocarbamate mix	2% pet.
8. Caine mix	7% pet.
9. Fradiomycin sulfate	20% pet.
10. Balsam of Peru	25% pet.
11. Rosin	20% pet.
12. Fragrance mix	8% pet.
13. Paraben mix	15% pet.
14. p-Phenylenediamine	1% pet.
15. Lanolin alcohol	30% pet.
16. p-Tert-butylphenol-formaldehyde resin	1% pet.
17. Epoxy resin	1% pet.
18. Primin	0.01% pet.
19. Urushiol	0.002% pet.
20. Sesquiterpene lactone mix	0.1% pet.
21. Potassium dichromate	0.5% aq.
22. Thimerosal	0.05% aq.
23. Formaldehyde	1% aq.
24. Kathon CG	0.01% aq.
25. Mercuric chloride	0.05% aq.

International Contact Dermatitis Research Group : ICDRG standard (? + : doubtful ; + : mild reaction, possible erythema, infiltration and papules ; ++ : Strong reaction, erythema, infiltration, papules and vesicles ; +++ : very strong reaction, intense erythema, infiltration and coalescing vesicles ; IR : irritant reaction ; NT : not tested). We defined + or more as positive. Fisher's exact test was used to compare results. P values less than 0.05 were considered statistically significant. Statistical analysis was performed using JMP 12 (SAS Institute, Inc., Cary, NC, USA).

Results

Patch Test Panel® (S) was used in 52 cases (mean age : 49 years, range 21-78 years ; 15 males and 37 females) (Fig. 1). JSA2008 was used in 235 cases (mean age : 50 years, range 7-85 years ; 42 males and 193 females). Among background diseases in Patch Test Panel® (S) cases, contact dermatitis was most common (19 cases, 36%), followed by metal allergy (14 cases, 27%) and atopic dermatitis (5 cases, 9%) (Fig. 2). Contact dermatitis was the most common background disease in both Patch Test Panel® (S) and JSA2008 cases.

Rates of positive PT results for each allergen are shown in Table 3. Among metal allergens, the rates of positive results for gold sodium thiosulfate and nickel sulfate were significantly higher for Patch Test Panel® (S) than for JSA2008. Rates of positive results for other allergens were not significantly different between the two methods.

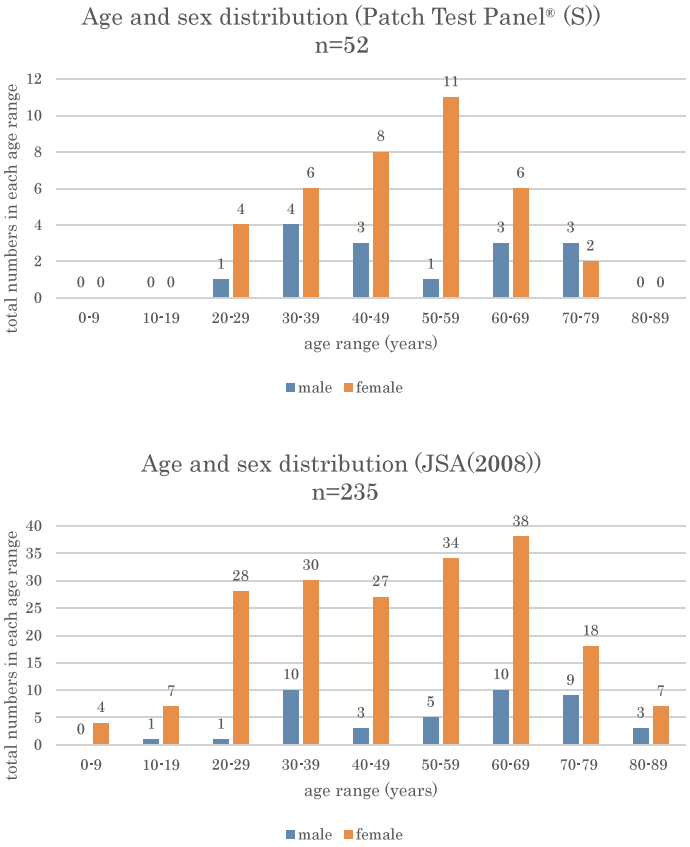

Fig. 1 Age and sex distribution in patch testing using Patch Test Panel®(S) and JSA2008

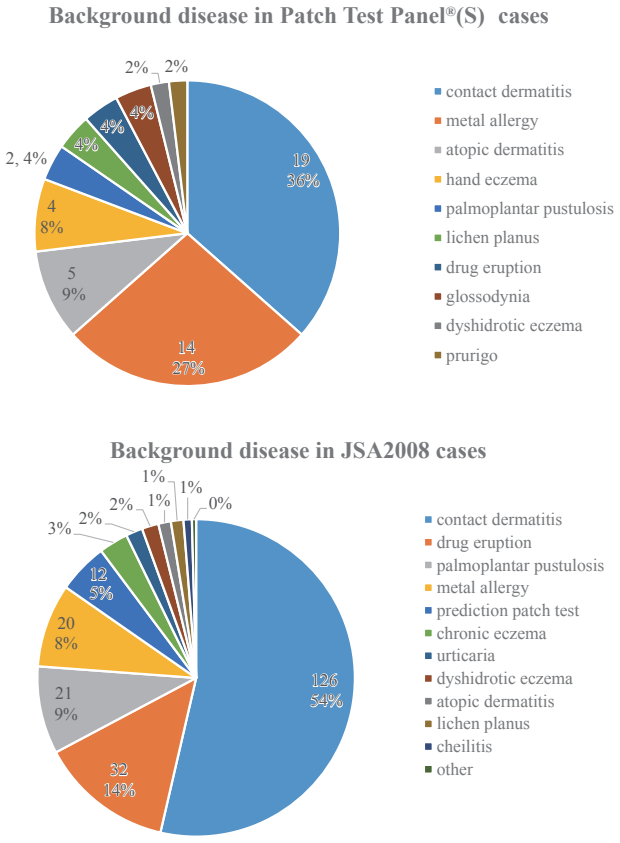

Fig. 2 Background disease in Patch Test Panel®(S) and JSA2008 cases

Table 3 Comparison of positive rates using Patch Test Panel®(S) or JSA2008.

	Patch Test Panel®(S) N=52	JSA2008 N=235	P value
1 Metal			
Cobalt chloride	8%	3.0%	0.118
Gold sodium thiosulfate	29%	1.3%	< 0.001
Nickel sulfate	27%	6.0%	< 0.001
Potassium dichromate	4%	11.9%	0.129
Mercuric chloride	NI	8.1%	
2 Rubber chemicals			
PPD black rubber mix	0%	1.3%	1.000
Thiuram mix	2%	3.4%	1.000
Mercapto mix	0%	0.4%	1.000
Dithiocarbamate mix	2%	0.9%	0.452
Mercaptobenzothiazole	0%	NI	
3 Medicaments			
Caine mix	0%	0.4%	1.000
Fradiomycin sulfate	2%	1.7%	1.000
4 Cosmetics			
Balsam of Peru	2%	3.8%	0.696
Fragrance mix	2%	6.0%	0.321
p-Phenylenediamine	6%	6.0%	1.000
Lanolin alcohol	2%	0%	0.181
5 Resin materials			
Rosin	0%	3.0%	0.357
p-Tert-butylphenol formaldehyde resin	2%	0%	0.181
Epoxy resin	0%	0.4%	1.000
6 Preservative materials			
Paraben mix	2%	1.3%	0.553
Thimerosal	2%	4.7%	0.701
Formaldehyde	0%	2.6%	0.596
Kathon CG	2%	1.3%	0.553
7 Plant materials			
Primin	NI	0.4%	
Urushiol	NI	7.2%	
Sesquiterpene lactone mix	NI	0.4%	

NI : not included, *Fisher's exact method

Discussion

In daily life, we are exposed to a variety of allergens. Contact with these allergens can induce allergic dermatitis in sensitized individuals[9]. Failure to identify a causative allergen can lead to an intractable clinical course[8]. Therefore, it is essential to identify causative allergens with PT[8]. JSA2008 includes 25 common allergens found in Japan and was widely used until 2015[9].

Patch Test Panel®(S) is a ready-to-apply PT package consisting of 22 common allergens, and has been covered by medical insurance since 2015[8]. As Patch Test Panel®(S) is convenient and time-saving, it is becoming more popular than JSA2008[8]. Compared to JSA2008, Patch Test Panel® (S) has uniform allergen dispersed in the unit, so it became possible to apply a certain

amount of allergen regardless of the skill of the operator. Therefore, we believe that the reliability to the test sample has increased. However, rates of PT positivity for each allergen have not been compared between Patch Test Panel® (S) and JSA2008 in patients in northern Kyushu.

Most allergens showed comparable positivity between the two methods, while gold sodium thiosulfate and nickel sulfate demonstrated much higher positive rates with Patch Test Panel®(S) compared to those with JSA2008. Nickel is a metal allergen with a high positive rate among JSA2008, and it is frequently contained in daily ornaments such as belt buckles and accessories[7]. In contrast, gold has a low ionization tendency and a high stability and resistance to corrosion, so that gold has been generally considered to hardly cause allergic reactions. However, gold allergy due to piercing is increasing and is received much attention[10]. Kanto also reported that the positive rate of gold sodium thiosulfate in Patch Test Panel® (S) was ten times higher than that in JSA2008[11]. Extensive revision is warranted to determine the optimum concentrations of gold sodium thiosulfate and nickel sulfate in Patch Test Panel®(S). The clinical relevance of high sensitivity to gold and nickel using this method requires further evaluation. It is necessary to accumulate and consider further cases of PT results with Patch Test Panel®(S).

Conflict of Interests

The authors have no conflicts of interest to declare.

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（和文抄録）

パッチテストパネル®（S）とジャパニーズスタンダードアレルゲンシリーズ（2008）を用いたパッチテスト結果の比較

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パッチテストは，治療抵抗性皮膚炎の原因を特定するのに有用である．2015 年まで広く使用されていたジャパニーズスタンダードアレルゲンシリーズ（2008）（JSA2008）は，私たちの身近にあってアレルゲンとなりうる可能性の高いものを集めた標準アレルゲンで，予期しない原因やアレルゲンを明らかにするために有用であり，PT を実施する場合，できるだけ JSA2008 の使用が推奨されてきた．加えて 2015 年以降，Patch Test Panel®（S）が日本で発売された．これは，22 種類の標準アレルゲンで構成されたすぐに使用できる ready-to-use の PT で，22 種類のアレルゲンのうち 21 種類が JSA2008 と同じであるため使いやすく，試薬調整も不要で時間節約となることなどから普及しつつある．

しかし，Patch Test Panel®（S）と JSA2008 を用いた北部九州に住む患者の PT 結果の比較は報告されていない．本研究では，九州大学病院，福岡歯科大学病院において JSA2008 と Patch Test Panel®（S）を用いた PT 結果を比較した．その結果，Patch Test Panel®（S）においては，JSA2008 と比較して，金チオ硫酸ナトリウム（$p < 0.001$）および硫酸ニッケル（$p < 0.001$）の陽性率が有意に高かった．これらの結果を今後，全国的な症例の蓄積をもとに，至適濃度の検討などに活かしていく必要があると考えた．

キーワード：パッチテスト，すぐに使える，パッチテストパネル（s），ジャパニーズスタンダードアレルゲン 2008