

References

1. García Pérez A, Condé Salazar L, Giménez Camarasa J M. *Tratado de dermatosis profesionales*, 1st edition. Madrid: Eudema, S. A. 1987: 403–405.
2. Peachey J E, Brien J F, Roach C A, Christopher W L. A comparative review of the pharmacological and toxicological properties of disulfiram and calcium carbimide. *J Clin Psychopharmacol* 1981; 1: 21–26.
3. Calnan C D. Cyanamide. *Contact Dermatitis Newsletter* 1970; 7: 150.
4. Black H. Contact dermatitis from lead cyanamide. *Contact Dermatitis* 1975; 6: 389.
5. Condé-Salazar L, Guimaraens D, Romero L, Harto A. Allergic contact dermatitis to cyanamide (carbodiimide). *Contact Dermatitis* 1981; 7: 329–330.
6. Fernández de Corrés L, Muñoz D. Allergic contact dermatitis to cyanamide. *Contact Dermatitis* 1982; 8: 346.
7. Goday Buján J J, Yanguas Bayona I, Soloeta Arechavala R. Allergic contact dermatitis from cyanamide: report of 3 cases. *Contact Dermatitis* 1994; 31: 331–332.
8. Torrelo A, Soria C, Rocamora A et al. Lichen planus-like eruption with esophageal involvement as a result of cyanamide. *J Am Acad Dermatol* 1990; 6: 1168–1169.
9. Kawana S. Drug eruption induced by cyanamide (carbimide): a clinical and histopathologic study of 7 patients. *Dermatology* 1997; 195: 30–34.

Value of patch tests in pristinamycin-induced drug eruptions

C. MAYENCE, A. DOMPMARTIN, L. VERNEUIL, M. MICHEL AND D. LEROY

Department of Dermatology, Centre Hospitalier Universitaire, Avenue Georges Clemenceau, 14033 Caen, France

Key words: pristinamycin; antibiotics; synergists; adverse drug reactions; acute generalized exanthematous pustulosis; virginiamycin; cross-sensitivity; positive patch test. © Munksgaard, 1999.

Patch testing is worthwhile in maculopapular (1, 2), eczematous (3) and pustular drug eruption (4, 5), because in approximately 20% of such patients the implicated drug is positive (6). The synergist antibiotic pristinamycin can induce adverse skin reactions (7–9).

Patients and Methods

Between 1989 and 1998, 11 patients (6 female, 5 male, mean age 51 years $\pm$ 16) presented with a cutaneous drug reaction after oral pristinamycin. All patients cleared after discontinuing the drug. 4 patients also had a history of contact dermatitis from virginiamycin. Imputability for pristinamycin was high (10), because it was the only drug recently introduced except in 2 patients. We had 30 patients in a control group (13 female, 17 male, mean age 67 years $\pm$ 15), who had all been treated with pristinamycin within the last 3 months without adverse reaction.

Patch tests were performed 1 to 3 months after treatment with pristinamycin. A tablet of pristinamycin (Pyostacine[®], Specia, Paris, France) was crushed and di-

luted 20% aq. and 20% pet. Other suspected drugs were also tested in 2 patients. Patch tests were performed with Finn Chambers on Scanpor (Epitest, Tuusula, Finland) and applied on the upper back. The tests were read 2 days later according to ICDRG guidelines.

Results

Of the 11 patients, 9 had a positive patch test to pristinamycin in aq. and pet. The pristinamycin test was the only one positive in the 2 patients who had taken other drugs. There was no relapse of the drug eruption during patch testing. Patch tests were negative in the 30 control patients (Table 1).

Discussion

The most frequent adverse effects of pristinamycin are cutaneous reactions (11). The 1st cases were reported in 1986 by Tomb & Grosshans (12) after local sensitization with virginiamycin. Bleumink & Nater (13), Lachapelle & Lamy (14), and Baes (15) had previously emphasized cross-reaction between virginiamycin and pristinamycin. We ascertained that 4 patients had previously used a topical preparation containing virginiamycin. Pristinamycin contains a well-known sensitizer, fraction IIA, which represents 45 to 60% of the molecular weight (16). The eruption may be a combination of an immediate-type and a delayed-type immune reaction. Eczematous lesions, and previous contact with virginiamycin, are in favour of systemic dermatitis (17).

It remains difficult to make an accurate diagnosis of drug-induced eruptions. In vitro tests are rarely reliable (18). Positive patch test results were obtained in 30% of patients presenting with a maculopapular drug rash (2).

Table 1. Patch test results

Cutaneous manifestations in patients treated with pristinamycin	No. patients tested	No. patients with positive pristinamycin patch tests
maculopapular rash	5	3
eczematous eruption	3	3
acute generalized exanthematous pustulosis	3	3
no eruption (controls)	30	0

The diagnostic value of patch testing is also good in eczematous reactions (6). In contrast, patch testing has weak sensitivity in Stevens-Johnson syndrome and erythema multiforme (19, 20). Many drugs, such as penicillin (2, 9), anticonvulsants (21, 22), histamine H1 antagonists (23), angiotensin-converting enzyme inhibitors (24), and corticosteroids (25), have been successfully patch tested. On the other hand, other drugs, such as the macrolides, are more difficult to test (9, 26).

Pristinamycin, which is mainly used in French-speaking countries, is easy to test (3, 7–9) and may be positive in the presence of diverse clinical features. Test concentrations range between 1 to 20% (6). For Barbaud et al. (9), a 30% dilution is the most appropriate. Water and petrolatum seem to be the best vehicles. To minimize the risk of relapse (27), patch tests should be performed well after the adverse cutaneous reaction, 6 to 12 weeks delay being recommended (6). The ideal control group is composed of patients previously treated with the drug without any cutaneous reaction. Ethical problems may arise because patch tests can sensitize patients in the control group (28). There is also a risk of relapse, which may be more severe than the original drug eruption (29). In 2 cases, patch tests were negative, which has rarely been observed (7, 9). Overall, our study confirms the value and reliability of pristinamycin patch tests.

References

1. Bruynzeel D P, Van Ketel W G. Skin tests in the diagnosis of maculo-papular drug eruptions. *Semin Dermatol* 1987; 6: 119–124.
2. Lisi P, Lapomarda V, Stingeni L, Assalve D, Hansel K, Caraffini S, Agostinelli D. Skin tests in the diagnosis of eruptions caused by betalactams. *Contact Dermatitis* 1997; 37: 151–154.
3. Michel M, Domp Martin A, Szczurko C, Castel B, Moreau A, Leroy D. Eczematous-like drug eruption induced by synergists. *Contact Dermatitis* 1996; 34: 86–87.
4. Moreau A, Domp Martin A, Castel B, Rémond B, Leroy D. Drug-induced acute generalized exanthematous pustulosis with positive patch tests. *Int J Dermatol* 1995; 34: 263–266.
5. Kempinaire A, De Raeve L, Merckx M, De Coninck A, Bauwens M, Roseeuw D. Terbinafine-induced acute generalized exanthematous pustulosis confirmed by a positive patch-test result. *J Am Acad Dermatol* 1997; 37: 653–655.
6. Bruynzeel D P, Maibach H I. Patch testing in systemic drug eruptions. *Clinics in Dermatology* 1997; 15: 479–484.
7. Bernard P, Fayol J, Bonnafoux A, Bedane C, Delrous J L, Catanzano G, Bonnetblanc J M. Toxidermies après prise orale de pristinamycine. *Ann Dermatol Venereol* 1988; 115: 63–66.
8. Barbaud A. Intérêt des patch tests aux médicaments dans le diagnostic des toxidermies (a propos de 3 cas). *Lettre du Gerda* 1993; 10: 28–32.
9. Barbaud A, Reichert-Penetrat S, Tréchet P, Jacquin-Petit M A, Ehlinger A, Noirez V, Faure G C, Schmutz J L, Béné M C. The use of skin testing in the investigation of cutaneous adverse drug reactions. *Br J Dermatol* 1998; 139: 49–58.
10. Moore N, Paux G, Begaud B, Biour M, Loupi E, Boismare F, Royer R J. Adverse drug reaction monitoring: doing it the French way. *Lancet* 1985; 2: 1056–1058.
11. Kernbaum S. Pristinamycin is a safe antibiotic. *Eur J Dermatol* 1993; 3: 244.
12. Tomb R, Grosshans E. Eczémas de contact et eczémas endogènes aux synergistes. *Lettre du Gerda* 1986; 3: 42–47.
13. Bleumink E, Nater J P. Allergic contact dermatitis to virginiamycin. *Dermatologica* 1972; 144: 253–256.
14. Lachapelle J M, Lamy F. On allergic contact dermatitis to virginiamycin. *Dermatologica* 1973; 146: 320–322.
15. Baes H. Allergic contact dermatitis to virginiamycin. False cross-sensitivity with pristinamycin. *Dermatologica* 1974; 149: 231–235.
16. Kernbaum S. Synergistes. *Sem Hôp Paris* 1985; 61: 2365–2371.
17. Truchetet F, Grosshans E, Brandenburger M. Les tests cutanés dans l'allergie médicamenteuse endogène. *Ann Dermatol-venereologique* 1987; 114: 989–997.
18. Kivity S. Fixed drug eruption to multiple drugs: clinical and laboratory investigation. *Int J Dermatol* 1991; 30: 149–150.
19. Wolkenstein P, Chosidow O, Fléchet M L, Robbiola O, Paul M, Dumé L, Revuz J, Roujeau J C. Patch testing in severe cutaneous adverse drug reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis. *Contact Dermatitis* 1996; 35: 234–236.
20. Gebhardt M, Wollina U. Allergy testing in serious cutaneous drug reactions – harmful or beneficial? *Contact Dermatitis* 1997; 37: 282–285.
21. Calkin J M, Maibach H I. Delayed hypersensitivity drug reactions diagnosed by patch testing. *Contact Dermatitis* 1993; 29: 223–233.
22. Alanko K. Patch testing in cutaneous reactions caused by carbamazepine. *Contact Dermatitis* 1993; 29: 254–257.
23. Michel M, Domp Martin A, Louvet S, Szczurko C, Castel B, Leroy D. Skin reactions to hydroxyzine. *Contact Dermatitis* 1997; 36: 147–149.
24. Cnudde F, Leynadier F, Dry J. Cutaneous reaction to captopril: value of patch tests. *Contact Dermatitis* 1990; 23: 375–376.
25. Mathelier-Fusade P, Marinho E, Aissaoui M, Mounedji N, Chabane M H, Leynadier F. Toxidermie à la prednisone et prednisolone. Intérêt des tests cutanés dans la recherche de réactions croisées. *Ann Dermatol-venereologique* 1996; 123: 453–455.
26. Igea J M, Quirce S, De la Hoz B, Fraj J, Pola J, Diez Gomez M L. Adverse cutaneous reactions due to macrolides. *Ann Allergy* 1991; 66: 216–218.
27. Machet L, Vaillant L, Dardaine V, Lorette G. Patch testing with clobazam: relapse of generalized drug eruption. *Contact Dermatitis* 1992; 26: 347–348.
28. Romano A, Di Fonso M, Pietrantonio F, Pocobelli D, Giannarini L, Del Bono A, Fabrizi G, Venuti A. Repeated patch testing in delayed hypersensitivity to beta-lactam antibiotics. *Contact Dermatitis* 1993; 28: 190.
29. Vaillant L, Camenen I, Lorette G. Patch testing with carbamazepine: re-induction of an exfoliative dermatitis. *Arch Dermatol* 1989; 125: 299.