Original Article

Topical dexketoprofen as a cause of photocontact dermatitis

R. López-Abad, Mª J. Paniagua, E. Botey, P. Gaig, P. Rodríguez, C. Richart.

Allergy Unit, Internal Medicine Department.
Hospital Universitari de Tarragona Joan XXIII, Tarragona (Spain).

Summary
We reported on the case of a patient who developed a cutaneous eruption in a photoexposed area 1 week after a continous topical treatment with dexketoprofen (Enangel®). Photopatch tests were positive for dexketoprofen, ketoprofen and piketoprofen and patch test was positive for piketoprofen. Control photopatch testing with dexketoprofen in 15 healthy volunteers was negative. Dexketoprofen, ketoprofen and piketoprofen are non-steroidal anti-inflamatory drugs (arylpropionic acid derivatives) often used as topical anti-inflammatory agents. It appears that the benzophenone moiety of their chemical structure is the cause of their photosensitivity and cross-photoreaction.

Key words: arylpropionic acid derivatives, cross-photoreaction, dexketoprofen, ketoprofen, non-steroidal anti-inflammatory drugs, photoallergic contact dermatitis, piketoprofen.

Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used as analgesic and antirheumatic agents. Since the 1970s these drugs are available for topical treatment of pain and inflammatory conditions. This form of treatment decreases the incidence of adverse systemic side-effects and increases the cutaneous side-effects. Propionic acid derivatives are the most frequent NSAIDs involved in these latest tipe of reactions, mainly of photocontact dermatitits [1].

Enangel® (topical dexketoprofen) was commercially introduced in November 1999. Dexketoprofen is a S(+)-enantiomer of ketoprofen and both are arylpropionic acid derivatives [2]. Contrary to ketoprofen, as far as we know, only one other case report of photocontact dermatitis due to dexketoprofen has been reported [3].

Case report

A 65-year-old woman was referred to our Allergy Unit for evaluation. In September 2001 she developed a pruritic erythema and blisters on her left ankle 1 week after the continous topical application of Enangel® (dexketoprofen trometamol 1.25%, Laboratorios Menarini, Barcelona, Spain) 2 x a day for joint pain. She had also been applying, at the same time and for the same reason, this gel on her right shoulder but no lesions appeared at this site.

She remembered a similar eruption 3 years earlier on her right hip some days after topical treatment for pain on this area with a non-steroidal anti-inflammatory drug (NSAID) although she could not remember which one. However, there was no other history of cutaneous eruptions, photosensitivity or drug sensitivity. The patient tolerated oral ibuprofen.

The lesions dissappeared leaving a moderate residual hyperpigmentation 15 days after discontinuing the Enangel® application and treatment with topical corticosteroid. Complete resolution was seen within the following 2 months.

Patch and photopatch tests (UVA 5J/cm2 at D2) were performed and their results are reported in Table 1. Constituents of Enangel® were supplied by the manufacturer. In order to elucidate cross-photoreaction with structurally-related compounds we carried out photopatch tests with other arylpropionic acid derivatives (APADs).

As shown in Table 1, the patient presented with positive results to: cobalt chloride and piketoprofen in

© 2004 Esmon Publicidad

Table 1. Results of patch and photopatch tests

		Patch tests		Photopatch
Allergens	% vehicle	D2	D4	D4
GEIDC standar series				NT
• Cobalt chloride		–	+	
• Rest of allergens		–	–	
Enangel®	as is	–	–	++++
NSAIDs series				
• Benzidamide chloride	1% pet.	–	–	NT
• Bufexamac	1% pet.	–	–	NT
• Diclofenac	1% pet.	–	–	NT
• Phenylbutazone	1% pet.	–	–	NT
• Indometacin	5% pet.	–	–	NT
• Paracetamol	0.1% pet.	–	–	NT
• Piroxicam	1% pet.	–	–	NT
• Thiosalicylic acid	0.1% pet.	–	–	NT
• Salicylic acid	1% and 5% pet	–	–	NT
APAD series				
• Ketoprofen	1% pet.	–	–	++++
• Piketoprofen	2% pet.	++	++	++++
• Ibuproxam	Nialen® ointment as is (ibuproxam 5%)	–	–	–
• Ibuprofen	5% pet.	–	–	–
• Naproxen	5% pet.	–	–	–
• Flurbiprofen	Froben® suppository as is (flurbiprofen 100 mg)	–	–	–
Components of Enangel®				
• Dexketoprofen	1 and 5% pet.	–	++++	++++
• Lavender essence	2% pet.	–	–	–
• Trometamol	1% aq.	–	–	–
• Ethyl alcohol 96%	as is.	–	–	–
• Carbomer	10% aq.	–	–	–

NT: not tested; D2: 48 hours after test application; D4: 96 hours after test application; GEIDC: Grupo Español de Investigación de Dermatitis de Contacto.

patch tests and dexketoprofen, ketoprofen and piketoprofen in photopatch tests.

We also performed control photopatch testing with dexketoprofen 1% and 5% pet. in 15 healthy volunteers with a negative result. These tests were necessary to rule out a simple phototoxic response.

Discussion

Arylpropionic acid derivatives (APADs) are non-steroidal anti-inflammatory drugs (NSAIDs) extensively used as topical and systemic anti-inflammatory agents. There are many reports in medical literature which report allergic contact dermatitis and photoallergic contact dermatitis as adverse reactions to these drugs [4-6], especially ketoprofen [7-11]. Some of these reports also say that the diphenylketone moiety (benzophenone) of ketoprofen plays a role in photocontact sensitivity, not so arylpropionic acid [9, 12-14]. This also explains the cross-photoreaction between ketoprofen and the other drugs such as fenofibrate, oxybenzone (benzophenone-3) and tiaprofenic acid which contain this group in their chemical structures [9, 12, 14, 15].

This case shows cross-photosensitivity between dexketoprofen, ketoprofen and piketoprofen, implicating the benzophenone structure. This has been recently

 © 2004 Esmon Publicidad

reported by Valenzuela et al [3]. The patient in our case reported also presented a contact sensitivity to piketoprofen that could be the cause of her previous episode on her right hip, and she also tolerated ibuprofen. This suggests that an arylpropionic acid structure is not responsible for cross-photoreaction and the different chemical characteristics of the compounds affect the tolerability and cross-sensitization of other drugs belonging to the same pharmacological group of the one causing the reaction. For this reason it is necessary to carry out an allergologic study to establish which drugs should be avoided.

Acknowledgements

We wish to thank to the Pharmacy Department of Hospital Universitari de Tarragona Joan XXIII, specially to Ana Bonet, for their helpful.

References

1. Ophaswongse S, Maibach H. Topical nonsteroidal antiinflammatory drugs: allergic and photoallergic contact dermatits and phototoxicity. Contact Dermatitis 1993; 29: 57-64.
2. Mauleon D, Artigas R, García ML, Carganico G. Preclinical and clinical development of dexketoprofen. Drugs 1996; 52 Suppl 5: 24-45.
3. Valenzuela N, Puig L, Barnadas MA, Alomar A. Photocontact dermatitis due to dexketoprofen. Contact Dermatitis 2002; 47 (4): 237.
4. Goday JJ, Oleaga JM, González M, Del Pozo J, Fonseca E. Photoallergic contact dermatitis from piketoprofen. Contact Dermatitis 2000; 43: 215.
5. Kawada A, Aragane Y, Maeda A, Yudate T, Tezuka T. Contact dermatitis due to flurbiprofen. Contact Dermatitis 2000; 42: 167.
6. Kurumaji Y, Oshiro Y, Miyamoto C, Keong C, Katoh T, Nishioka K. Allergic photocontact dermatitis due to suprofen. Photopatch testing and cross-reaction study. Contact Dermatitis 1991; 25: 218-223.
7. Miralles JC, Negro JM, Sánchez-Gascón F, García M. Contact dermatitis due to ketoprofen with good tolerance to piketoprofen. Allergol Inmunol Clin 2001; 16: 105-108.
8. García MT, Matheu V, Pérez A, Díaz MP, Martínez MI, Zapatero L. Contact Photodermatitis due to Ketoprofen and Piketoprofen. Allergol Inmunol Clin 1999; 14: 148-150.
9. Matsusuhita T, Kamide R. Five cases of photocontact dermatitis due to topical ketoprofen: photopatch testing and cross-reaction study. Photodermatol Photoimmunol Photomed 2001; 17: 26-31.
10. Kawada A, Aragane Y, Asai M, Tezuka T. Simultaneous photocontact sensitivity to ketoprofen and oxybenzone. Contact Dermatitis 2001; 44. 370.
11. Albès B, Marguery MC, Schwarze HP, Journé F, Loche F, Bazex J. Prolonged photosensitivity following contact photoallergy to ketoprofen. Dermatology 2000; 201: 171-174.
12. Sugiura M, Hayakawa R, Xie Z, Sugiura K, Hiramoto K, Shamoto M. Experimental study on phototoxicity and the photosensitization potential of ketoprofen, suprofen, tiaprofenic acid and benzophenone and the photocross-reactivity in guinea pigs. Photodermatol Photoimmunol Photomed 2002; 18: 82-89.
13. Sugiura M, Hayakawa R, Kato Y, Sugiura K, Ueda H. 4 cases of photocontact dermatitis due to ketoprofen. Contact Dermatitis 2000; 43: 16-19.
14. Le Coz C, Bottlaender A, Scrivener J, Santinelli F, Cribier B, Heid E, Grosshans M. Photocontact dermatitis from ketoprofen and tiaprofenci acid: cross-reactivity study in 12 consecutive patients. Contact Dermatitis 1998; 38: 245-252.
15. Horn HM, Humphreys F, Aldridge D. Contact dermatitis and prolonged photosensitivity induced by ketoprofen and associated with sensitivity to benzophenone-3. Contact Dermatitis 1998; 38: 353.

Dra. Raquel López Abad

Allergy Unit
Hospital Universitari de Tarragona Joan XXIII
C/ Dr. Mallafré Guasch, 4
43007 Tarragona (Spain)
Tel.: +34 9777 29 58 99 - Ext 2215
Fax: +34 977 29 58 35
E-mail: alergia@hjxxiii,scs,es

© 2004 Esmon Publicidad