

Photopatch testing negative in systemic quinine phototoxicity

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Summary

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Drug-induced phototoxicity can be caused by topical or systemic agents and is diagnosed on the basis of clinical history, examination and appropriate investigations. Photopatch testing is the investigation of choice for topical photocontact allergic dermatitis, but its use in drug-induced phototoxicity has not been validated. We retrospectively analyzed the results of photopatch testing to the drug quinine sulfate in three patients in whom a diagnosis of drug-induced phototoxicity to this agent had been made. None of the three patients had positive photopatch test reactions at any time point. This demonstrates that in our patients, photopatch testing to quinine sulfate was not a useful additional investigation for diagnosing drug-induced phototoxicity.

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Conflicts of interest:

None declared.

Drug-induced phototoxicity is a non-immunologically mediated process, which can lead to a photo-exposed skin site eruption. It can be caused both by medications applied topically and administered systemically where there is subsequent exposure to ultraviolet (UV) and/or visible light. The diagnosis of drug-induced phototoxicity requires an accurate temporal history of when a drug has been taken in relation to the onset of symptoms and signs, clinical examination and appropriate investigations. Among investigations employed, monochromator phototesting may show delayed sensitivity to UV (often UVA) and/or visible light, while a skin biopsy may show apoptotic 'sunburn cells', epidermal necrosis or a lichenoid pattern (1). Photopatch testing is the investigation of choice for topical photoallergic contact dermatitis, which can resemble drug-induced phototoxicity clinically, but its role in drug-induced phototoxicity has not been validated. We sought to determine whether photopatch testing to the drug quinine sulfate, which has known phototoxic properties, could contribute to making a diagnosis of drug-induced phototoxicity.

We retrospectively analyzed the results of photopatch testing to quinine sulfate in three patients in whom a diagnosis of drug-induced phototoxicity to quinine sulfate had been made. Photopatch testing was performed on the skin of the back according to the European consensus methodology (2). The quinine sulfate was prepared in both petrolatum and water for two patients and in petrolatum alone for one patient. Duplicate sets were applied for 24 h before irradiation of one set with UVA.

In two of the three patients, their UVA sensitivity was such that 5 J/cm² could not be used and a lower dose was employed. Readings of the photopatch test site were made at 24 and 48 h after irradiation and any reactions seen were recorded using the ICDRG grading scale. All three patients also underwent monochromator phototesting as part of their investigations, one of whom had this repeated after 4 months. A skin biopsy was performed in one patient.

The characteristics of the three patients and results of their investigations are summarized in Table 1. None of the three patients had positive photopatch test reactions to quinine sulfate at any time points.

Patient 1 presented with a 10-year history of dermatitis on the dorsae of the hands, with a sharp cut-off at the clothing line of her wrist evident on examination. She reported a worsening of her skin between spring and autumn, with improvement in the winter months. Following investigation, she was unable to discontinue quinine sulfate due to ongoing nocturnal leg cramps but she was able to reduce the dose. When she was reviewed at the clinic 6 months after her investigations, she reported improvement of her dermatitis. Patient 2 presented with a lichenoid rash on photo-exposed sites and stopped quinine sulfate following her investigations. This led to rapid resolution of the rash clinically and when repeat monochromator phototesting was performed after 4 months, she had normal delayed responses. Patient 3 presented with a lichenoid rash on photo-exposed sites in the summer months with an onset 3

Table 1. Summary of patient characteristics and investigation results

Patient	Age (years) and sex	Duration quinine taken (months)	Duration off medication at time of investigation (months)	Concentrations and vehicles of quinine used in photopatch testing	Dose of UVA used for photopatch test irradiation (J/cm ²)	Photopatch test result	Monochromator wavelength sensitivity	Repeat monochromator wavelength sensitivity	Skin biopsy result
1	76, female	120	Still on	1%, 5% and 30% in pet + 1% in aqua	5	Negative	None	Not done	Not done
2	80, female	18	Still on	1%, 5% and 30% in pet + 1% in aqua	0.25	Negative	UVA	None (repeated after 4 months)	Lichenoid dermatosis
3	66, female	3	6	1%, 5% and 30% in pet	1.8	Negative	UVA and visible	Not done	Not done

months after commencing quinine sulfate. At this point she discontinued the drug. Following her investigations, she remained off the drug and when contacted 4 months later, declined further follow-up due to resolution of her rash.

Because of quinine sulfate's known phototoxic properties, it is likely that if a higher dose of UVA and/or higher concentration of drug had been employed during photopatch testing, some positive phototoxic reactions may have resulted (3). However, the relevance of such skin reactions to the systemic administration of the medication would not have been clear, as a direct phototoxic effect on the skin cannot be interpreted as equivalent to systemic phototoxicity due to the different mechanisms potentially involved. Positive photopatch test results to systemically administered drugs have also been cited as supportive evidence when diagnosing systemic photoallergic contact dermatitis (4, 5). However, it is possible that some of these results may have been due to false-positive phototoxic reactions.

We have demonstrated negative photopatch testing to quinine sulfate in three patients in whom a final diagnosis of drug-induced phototoxicity following oral ingestion of quinine sulfate was made. Photopatch testing was not a useful investigation in

arriving at this diagnosis. In these cases, the final diagnosis was made by considering the clinical history, examination and all investigation results, including normalization of repeat monochromator phototesting after discontinuation of quinine in one patient.

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