

DRUG INDUCED PHOTOSENSITIVITY

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Summary

Photosensitivity due to various drugs have been observed. The incidence of drug induced photosensitivity was studied among 2875 patients and was found to occur in 16 cases (0.56%). Sulphadimidine, demethylchlor tetracycline and promethazine were incriminated as the etiological agents. Various drugs and their photosensitivity potential are discussed with a review of the literature.

Normal response of the skin to ultra violet light (U.V.L.) in the spectrum range between 280 nm and 320 nm is erythema which appears about 6 hours after exposure and reaches maximum intensity after approximately 24 hours. The minimal erythema dose (M.E.D.) is defined as that amount of ultra violet rays (U.V.R.) required to produce a barely perceptible erythema over the skin 24 hours after exposure.

Systemic photosensitivity is often caused by drugs which may be ingested, injected, inhaled or absorbed through skin or mucous membranes of conjunctivae, mouth or nose. The chemical reaches skin via circulation; the clinical features of eruptions being either phototoxic or photoallergic in nature. Distinction between phototoxic and photoallergic type of sensitivity reactions is not always clear. Precisely, phototoxic reaction is one of quantitative and not qualitative alteration but reactions of qualitative alteration are often allergic.

Review of literature

Systemic photosensitivity is often caused by drugs such as sulphonamides^{1,2}, its derivatives chlorthiazides, hydrochlorthiazide and hypoglycaemic agents³⁻⁵; demethylchlortetracycline⁶⁻¹⁰, tetracycline, oxytetracycline¹¹⁻¹³, phenothiazines, chlorpromazine¹⁴⁻¹⁶, promethazine¹⁷, cyclophosphamide¹⁸, griseofulvin¹⁹ and diphenhydramine hydrochloride²⁰. Other drugs which can cause photosensitivity are isoniazid, furocoumarines, heavy metals, stilbestrol and barbiturates²¹.

The photosensitivity potential of demethylchlortetracycline has been studied by earlier workers using different dosage schedules. It was found that with daily doses of 300 to 450 mgm no reactions occurred. With 600 mgm daily⁹ reactions were noticed (19). These were of a phototoxic nature⁹. Photosensitivity reactions has been reported to be less frequent with tetracycline and oxytetracycline as compared to those with chlortetracycline and demethylchlortetracycline¹³. Cullen et al¹³ estimated quantitative cutaneous and serum levels of the drug and found this concentrated in the areas of dermatitis. Lamb et al¹⁹

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observed erythema in 9 out of 15 cases of tinea infection treated with griseofulvin but Blank and Roth²² did not observe any such reaction. Mulay et al²³, Sehgal²⁴, Kapur²⁵ used griseofulvin in cases of herpes zoster, lichen planus and molluscum contagiosum and did not notice any photosensitivity reaction.

There is a cross sensitivity between Chlorpromazine and promethazine. Chlorpromazine produces both photo-toxic and photoallergic reactions^{15, 16, 20}. Photoallergic reactions induced by phenothiazine such as trimeprazine (Vallergan) and promethazine (Phenargan) are at present very frequent²¹. Photosensitivity is rare with barbiturates and isoniazid²¹.

Material and Method

Various drugs known to cause photosensitivity reactions such as sulphadimidine, griseofulvin F.P., tetra and oxytetracycline, promethazine, chlorpromazine, phenobarbitone and isoniazid were prescribed to 2875 individuals in the Indian Armed Forces personnel or their dependents for various ailments during periods between July 1974 and December 1976. The drugs were given in conventional doses and duration. Isoniazid and chlorpromazine were prescribed for prolonged periods for indoor cases with pulmonary tuberculosis and psychiatric illness respectively. Almost all the patients excepting those admitted to psychiatric and T.B. wards were performing their normal duties during period of treatment. No restrictions were put on these patients with regard to sun exposure. Driving of vehicles or working in front of fire was prohibited in those who were taking phenobarbitone, griseofulvin and promethazine.

This study reveals that incidence of photosensitivity among 2875 (0.56%) cases treated with various potentially photosensitising drugs is low.

Discussion

Photosensitivity reactions due to sulphadimidine or its derivatives were reported with sulphonamides¹, sulphapyridine²⁶, sulphamethoxydiazines², chlorthiazide and hydrochlorthiazide^{4, 27}. Photosensitizing action of the phenothiazine compounds is related to the presence of chloride ion in the number two position in phenothiazine nucleus⁵. Eight (0.85%) cases in our series developed photosensitivity with sulphadimidine (sulphamezathine). Demethyl chlortetracycline (Ledermycin) induced photosensitivity in 6 (1.3%) out of 467 cases. All of them were receiving 300 mg of the drug twice a day and developed erythema over sun exposed areas for the first time on the third or fourth day of therapy. Cahn et al⁹ observed photosensitivity in 28.4% of cases who were on a dosage of 600 mg per day. None of his cases taking smaller doses of 300 to 450 mg per day developed any reaction. None of the 565 cases receiving tetracycline or oxytetracycline developed photosensitivity, even though in 12 cases a dosage was of 2 gm daily was given for 20 days. This study thus confirms the views of Cullen et al¹⁸ that photosensitivity of tetracycline and oxytetracycline are much less than that of chlorthiazide and demethylchlortetracycline. There was no photosensitivity reaction among 339 cases of tinea infection treated with griseofulvin F.P. It appears that griseofulvin is not a common cause of photosensitivity. 2 (0.8%) out of 238 patients developed photosensitivity towards promethazine but none with chlorpromazine. There was also no incidence of photosensitivity among patients receiving isoniazid and phenobarbitone. This study confirms the opinion of Sam²⁸ that the individual predisposition plays a role in the production of photosensitivity reactions. It is interesting to note that among 669 cases with various other dermatitis treated by the author during the period

of present study 83 (12.5%) had sunburns. They were soldiers who were performing their normal duties in varied environments. All of them had developed their lesions for the first time and denied history of consuming any known photosensitivity drugs or using any local application, known to have a photosensitising effect.

Treatment

Most of the cases of photosensitivity and sunburns were hospitalized and were treated with antihistamines, sun screens and local corticosteroids. Systemic corticosteroids were prescribed in severe cases. Triprolidine hydrochloride (Actidil) was found to be superior to pheniramine maleate and cyproheptadine hydrochloride.

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References :

1. Epstein S: Photoallergy and primary photosensitivity to sulphonamide *J Invest Derm*, 2 : 43, 1939.
2. Walters JW: Photosensitization (Madribon), *Arch Derm*, 85 : 666, 1962.
3. Harber LC, Lashinsky AM and Baer RL : Photosensitivity due to Chlorthiazide and hydrochlorthiazide, *N Eng J Med*, 261 : 1378, 1958.
4. Norins S: Chlorthiazide drug eruptions involving photosensitization, *Arch Derm*, 79 : 592, 1959.
5. Sams WM: Photosensitizing therapeutic agents *JAMA*. 174 : 2043, 1960.
6. Harris HJ; Aureomycin and chloramphenicol in brucellosis with special reference to side effects, *JAMA*, 142 : 161, 1950.
7. Falks MS: Light sensitivity due to demethyl chlortetracycline *JAMA*, 172 : 1156, 1960.
8. Fuhrman DL and Drowns B: Demethyl chlortetracycline the clinical aspects of its use in *Dermatology*. *Arch Derm*, 82 : 244, 1960.
9. Cahn NM, Levy EJ and Mc Millen JA : Nature and incidence of photosensitivity reactions to demethylchlortetracycline, *Arch Derm*, 84 : 485, 1961.
10. Orentreich N, Harber LC and Tromovitch TA : Photosensitivity and photo-onycholysis due to demethylchlortetracycline, *Arch Derm*, 83 : 730, 1961.
11. Segal BM: Photosensitivity, nail discoloration and onycholysis (side effects of tetracycline therapy), *Arch Intern Med*, 112 : 165, 1963
12. Tromovitch TA and Jacobs PH: Photosensitivity to oxytetracycline, *Ann Intern Med*, 58 : 529, 1963.
13. Cullen SI, Cataland PM and Helfman RJ: Tetracycline sun sensitivity. *Arch Derm*, 93 : 77, 1966.
14. Schultz KH, Wiskemann A and Wulf K : Clinical and experimental investigations on photo dynamic effects of phenothiazine derivatives, particularly of chlorpromazine, *Arch Klin Exp Derm*, 202 : 285, 1956.
15. Cahn NM and Levy EJ : Ultra violet light factor in chlorpromazine dermatitis, *Arch Derm*, 75 : 38, 1957.
16. Epstein JH, Brunsting LA, Petersen MC, et al : Study of photosensitivity occurring with chlorpromazine therapy, *J Invest Derm* 28 : 329, 1957.
17. Epstein S and Row RJ : Photoallergy and photo cross sensitivity to phenergan, *J Invest Derm*, 29 : 319, 1957.
18. Kapur TR : Systemic photosensitivity towards cyclo phosphamide (Endoxan), *Indian J Derm Vener Lep* 42 ; 5, 1976.
19. Lamb JH, Jones PE, Morgan RJ, et al : Further studies in light sensitive eruptions *Arch Derm*, 83 : 566, 1961.
20. Schreiber MM and Naylor LZ : Antihistamine photosensitivity, *Arch Derm*, 86 : 58, 1962.

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21. Rook AJ, Wilkinson DS and Ebling FJG : Text Book of Dermatology, 1st Ed, Blackwell Scientific Publications Oxford, 1969 p 379, 390.
 22. Blank H and Roth FJ: The treatment of dermatomycosis with orally administered griseofulvin, Arch Derm, 79 : 259, 1959.
 23. Mulay DN, Sood BK and Ahuja BB : Value of griseofulvin in treatment of Herpes Zoster, Indian J Derm Vener, 38 : 65, 1972.
 24. Sehgal VN : Further evaluation of griseofulvin therapy in Lichen planus, Indian J Derm Vener, 38 : 107, 1974.
 25. Kapur TR : Griseofulvin F.P. therapy in molluscum contagiosum, Indian J Derm Vener Lep 42 : 289, 1976.
 26. Perry HO and Winkelmann RK : JAMA, 111 : 127, 1959. (Quoted by No. 21).
 27. Harber LC, Lashinsky AM and Baer RL : Skin manifestations of photosensitivity due to chlorthiazide and hydrochlorthiazide, J Invest Derm, 33 : 83, 1959.
 28. Sams WM : Contact photodermatitis, Arch Derm, 73 : 142, 1956.
 29. *Kapur TR and Chopra TR : Normal and abnormal reactions of human skin to light Med J Armed Forces (India). 33:510, 1977.
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- * This article has not been quoted as reference but consulted while writing this article.

TRUE

Study of epitrichial (apocrine) gland function in the human axilla is difficult; the monitoring of their output is complicated by the presence of atrichial gland and by the fact that they produce relatively small quantities of sweat often only intermittently. The effect of aluminium chlorhydrate was therefore tested on the epitrichial sweat glands of cattle; the output of which can be accurately quantitated with a view to obtaining comparative information of potential relevance to man.

Topical application of aluminium chlorhydrate had no appreciable antipersipant action on epitrichial (apocrine) glands of cattle. This may indicate that the salt failed to penetrate to the glands. Application of aluminium salts over a long period of time could perhaps result in penetration of sufficient aluminium to cause superficial inflammation and possibly sweat gland damage.

The comparative evidence lends support to the view of Shelley and Hurley that aluminium salts have no significant antiperspirant action on the epitrichial glands of human axilla. It is probable that aluminium chlorhydrate is an effective antiperspirant only on the atrichial glands. This implies that the deoderent activity of aluminium chlorhydrate in the axilla is not an indirect result of a reduction in sweat output from the eptrichial glands but a direct result of antibacterial properties and its action in reducing the quantity of sweat from the atrichial glands.

Reference : Rees-Jones AM and Jenkinson DM : The effect of aluminium chlorhydrate on sweat gland activity in cattle, J Invest Dermatol, 70 : 134, 1978.