Acta Derm Venereol (Stockh) 1985; 65: 93–96

Single Exposure to Ultraviolet Irradiation and Elicitation of Human Allergic Contact Dermatitis

PETER SJÖVALL, OLE B. CHRISTENSEN and HALVOR MÖLLER

Department of Dermatology, Lund University, General Hospital, Malmö, Sweden

Sjövall P, Christensen OB, Möller H. Single exposure of ultraviolet light and elicitation of human allergic contact dermatitis. Acta Derm Venereol (Stockh) 1985; 65: 93–96.

Ultraviolet radiation has been stated to inhibit afferent as well as efferent phases of allergic contract dermatitis. In this controled study 17 female patients with nickel allergy were studied by three different protocols after an initial determination of their degree of hypersensitivity. They were patch tested with nickel sulfate immediately after UVB, 4-6 days after UVB, or immediately after external PUVA. Neither depressing nor enhancing of the allergic reaction was observed when compared to non-irradiated controls. The role of Langerhans cells as antigen-presenting cell playing an important role in the elicitation phase of allergic contract dermatitis is discussed and questioned. *Key words: Ultraviolet irradiation; Contact allergy.* (Received June 13, 1984.)

O. B. Christensen, Department of Dermatology, General Hospital, S-21401 Malmö, Sweden.

The effect of ultraviolet radiation (UVR) on induction and elicitation of allergic contact dermatitis has attracted attention during the last few years (1, 2, 3, 4, 5, 6, 7, 8). Restricting our interest to the effect of UVR on the efferent phase of allergic contact dermatitis it has been shown that both UVB (290–320 nm) and PUVA (psoralens+UVA (320–400 nm)) applied before elicitation, decreased the intensity of experimental allergic contact reactions in the guinea pig (1, 2, 4, 5, 6). Concerning the influence of PUVA on the elicitation phase of allergic contact dermatitis in humans, two pilot studies have been published indicating, that the intensity of a challenge reaction is decreased (7, 8). Human experimental studies involving the influence of UVB on the efferent phase of allergic contact dermatitis have, to our knowledge, not been published. However, a clinical study has recently shown beneficial effect of UVB when treating patients with chronic allergic contact dermatitis of the hands (8, 9).

The aim of the following experimental study is to elucidate the possible effect of UVB and PUVA on the intensity of the efferent phase of an allergic contact dermatitis in humans.

MATERIAL AND METHODS

Subjects

Seventeen female subjects (Mean age 32 years, range 17–52 years) hypersensitive to nickel as proved by earlier patch testing were enrolled in the study.

Primary hypersensitivity screening

To determine the degree of individual hypersensitivity, the left side of the buttocks in each subject was patch tested (Finn Chamber technique on Scanpor) with a serial dilution of $NiSO_4$ ($6H_2O$) in distilled water with the following concentrations, 1.6 %, 0.8 %, 0.4 %, 0.2 % and 0.1 %. The tests were applied for 48 hours and read 24 hours later. In each subject we determined the lowest nickel concentration resulting in a uniform infiltrated erythematous reaction with papules. This concentration was named the "minimal eczematous concentration" (MEC) and was used throughout the study.

Determination of minimal erythema dose (MED) and minimal phototoxic dose (MPD)

At the same time as the MEC determination, we examined the MED reaction in 12 subjects by applying 5 different doses of UVB to 1 cm^2 areas on the left buttock. The light source was a xenon arc lamp (XBO 150 W, Osram, Germany) emitting a continuous spectrum from 240 nm to about 400 nm after which there is less flux until the infrared region. The reactions were read 24 hours later and MED was defined as the lowest dose of UVB resulting in a homogenous well marginated erythema.

In the 5 remaining subjects the MPD was determined by applying 8-methoxypsoralen (0.2% in absolute ethanol) for 15 minutes on an area of 10×15 cm on the left buttock. After removal of the psoralen the area was covered with a plastic slip with 4 holes, 1 cm^2 each. The areas were then exposed to 0.25, 0.5, 1.0 and 2.0 joules, respectively, of long wave ultraviolet light from a PUVA 4000 (Waldmann AG, Schwenningen, GFR). MPD was defined 72 hours later as the lowest dose of UVA resulting in a homogenous well marginated erythema.

Design of the study

Immediately after the primary MEC, MED and MPD determination the study was divided in three parts.

I. UVB immediately prior to retesting. In 6 subjects UVB doses of 0.5, 1.0, 2.0 and 4.0 MED to 1 cm^2 areas were given to the right buttock. Immediately after this exposure an MEC nickel patch test was applied to these areas for 48 hours. As control served an identical patch test in a non-irradiated area on the right buttock. Twentyfour hours after removal of the patches the tests were read and the intensity of the test reaction on irradiated areas was compared to that of the non-irradiated control site. The control test area served as reference and was arbitrarily assigned a ++ value. If the test reactions on the irradiated areas were stronger or weaker they were given a +++ or + value, respectively.

II. *UVB 4–6 days prior to retesting.* In 6 subjects the same procedure as under I was followed, with the exception that the MEC nickel patches were applied 4–6 days after UVB exposure.

III. *External PUVA immediately prior to retesting.* In the remaining 5 subjects 3 areas of 1 cm^2 each were exposed to external PUVA in the doses 0.5, 1.0 and 2.0 MPD according to the method mentioned above. Immediately thereafter MEC nickel patches were applied to the irradiated areas and a control site. Otherwise the test method and reading did not differ from procedures under I and II.

RESULTS

In Table I illustrating the eczematous reactions after UVB exposure immediately before retesting some differences may be seen in the reaction intensity between the 6 subjects tested. Summarizing the scores induced with different UVB doses, however, the sums do not deviate from non-exposed skin. In principle, the same result was obtained with the protocol using UVB 4–6 days before retesting and that using PUVA immediately before retesting.

Table I. *Strength of nickel patch tests exposed to 0.5–4.0 MEd of UVB just before application*

The non-irradiated test reactions (control) were given a ++ value, a weaker or stronger reaction a + or a +++ value, respectively. The sum of + for each patient and for each UVB dose is given in the margin

Subject	Control	0.5 MED	1.0 MED	2.0 MED	4.0 MED	Σ+
1	++	+	+	+++	+++	10
2	++	++	++	+++	+++	12
3	++	++	+++	+++	+++	13
4	++	++	++	+	+	8
5	++	++	++	++	++	10
6	++	++	++	++	++	10
	12	11	12	14	14	Σ+

DISCUSSION

As a consequence of earlier reports where both UVB and PUVA showed some depressive effect of the elicitation phase of allergic contact dermatitis in guinea pigs (1, 2, 4, 5, 6) we chose to investigate the possible effect of these two light exposure modalities in humans. We were, however, unable to confirm these positive results in our protocols, neither when UVB nor when PUVA was applied. Obviously, different reasons have to be taken into account when evaluating our negative results. First of all the total dose of UVR and relationship between UVR exposure and hapten application have to be considered. In the experimental animal studies several exposures during about 2 weeks resulting in a rather high total dose were applied (1, 2, 4, 5, 6). Also long term exposure of PUVA was applied in two human pilot studies (7, 8) to influence the elicitation phase of allergic contact dermatitis. Langerhans' cells (LC) have been implicated to take active part in the elicitation of allergic contact dermatitis (10, 11). Several studies indicate that UVR exposure affects LC (12, 13, 14). Aberer et al (12) and Gilcreast et al (13) have shown an almost total depletion of LC, defined by loss of ATP-ase activity and Ia positivity, as well as damage to LC shown by electron microscopy 24 hours after a single exposure of 1–3 MED to human skin. In our two UVB protocols we applied our hapten (nickel) immediately and 4–6 days after irradiation, respectively. At the time when nickel is presented to LC the antigen presentation ability of LC might very well be impaired by UVR. However, it can not be excluded that the hapten has obtained full antigen capacity before LC damage occurs when nickel and UVB are applied simultaneously (protocol 1). From a theoretical point of view it is possible that LC damage might be repaired before antigen presentation takes place as in protocol 2. If these presumptions are correct we are not able, in our investigation, to determine the role of LC in the elicitation of allergic contract dermatitis. However, it is reasonable to believe that we at least in one of our two protocols have applied the hapten when LC are damaged. Therefore our results indicate that LC perhaps do not play an active role during elicitation of allergic contact dermatitis. As a matter of fact, the role of LC in the elicitation phase of allergic contact dermatitis has been questioned in other studies (15, 16). Macrophages seem to play a more active part than LC (15) and the vehicle has been shown to activate LC to the same degree as hapten in allergic patch test reactions (16).

PUVA affects the density of LC in guinea pigs as well as in humans (4, 17, 18, 19). To our knowledge it is unknown how fast this happens after PUVA exposure. In our protocol 3 it is likely that the hapten has obtained full antigen capacity before PUVA damages LC. More extended studies in humans are needed to investigate a possible depressive effect of PUVA and its mechanisms on the elicitation of allergic contact dermatitis.

Another factor to be considered when comparing our present results to earlier investigations is the ratio between the size of UV irradiated areas and patch test areas. Generally the UV irradiated areas have been much larger in earlier investigations than in our study, in which UVR and test areas were of approximately the same size. We do not know whether this factor is of crucial importance or not, but a correct judgement of the relationship of size between UVR and test areas requires further investigations.

REFERENCES

1. Morison W, Parrish JA, Woehler ME, Block KL. The influence of ultraviolet radiation on allergic contract dermatitis in ghe guinera pig. I. UVB radiation. Br J Dermatol 1981; 104: 161–164.
2. Morison W, Parrish JA, Woehler ME, Block KL. The influence of ultraviolet radiation on allergic contact dermatitis in the guinea pig. II. Psoralene–UVA radiation. Br J Dermatol 1981; 104: 165–168.
3. Strauss GH, Greaves M, Price M, Bridges BA, Hall-Smith P, Vella-Briffa D. Inhibition of delayed

hypersensitivity reaction in skin (DNCB test) by 8-methoxypsoralen photochemoterapy. Lancet 1980; ii: 556–559.
4. Horio T, Okamoto H. The mechanisms of inhibitory effect of 8-methoxypsoralen and longwave ultraviolet light on experimental contact sensitization. J Invest Dermatol 1982; 78: 402–405.
5. Austad, J, Mørk NJ. Effects of PUVA on delayed hypersensitivity in the guinea pig. Br J Dermatol 1981; 105: 641–644.
6. Austad, J, Mørk NJ. Effects of short-wave ultraviolet light (UVB) on delayed hypersensitivity in the guinea pig. Acta Derm Venereol (Stockh) 1982; 62: 133–136.
7. Thorvaldsen, J, Volden G. PUVA-induced diminution of contact allergic and irritant skin reactions. Clin Exp Dermatol 1979; 5: 43–46.
8. Jansén CT, Viander M, Kalimo K, Soppi AM, Soppi E. PUVA treatment in chromiumhypersensitivity: Effect on skin reactivity and lymphocyte functions. Arch Dermatol Res 1981; 270: 255–261.
9. Mørk NJ, Austad J. Short-wave ultraviolet light (UVB) treatment of allergic contact dermatitis of the hands. Acta Derm Venereol (Stockh) 1983; 63: 87–89.
10. Silberberg-Sinakin I, Thorbecke JG: Contact hypersensitivity and Langerhans cells. J Invest Dermatol 1980; 75: 61–67.
11. Mackie RM, Turbitt ML. Quantitation of dentritic cells in normal and abnormal human epidermis using monoclonal antibodies directed against Ia andHTA antigens. J Invest Dermatol 1983; 81: 216–220.
12. Aberer W, Schuler G, Stingl G, Hönigsmann H, Wolff K. Ultraviolet light depletes surface markers of Langerhans cells. J Invest Dermatol 1981; 76: 202–210.
13. Gilcrest B, Murphy G, Soter N. The effect of chronologic aging and ultraviolet irradiation on Langerhans cells in human epidermis. J Invest Dermatol 1982; 79: 85–88.
14. Bergstresser P, Toews G, Strelein W. Natural and perturbed distributions of Langerhans cells: Responses to ultraviolet light, heterotopic skin grafting and dinitrofluorobenzene sensitization. J Invest Dermatol 1980; 75: 73–77.
15. De Panfilis G, Gianotti B, Manara GC, Lombardo-Demonici L, Ferrari C, Cappugi P. Macrophage–T lymphocyte relationships in man's contact allergic reactions. Br J Dermatol 1983; 109: 183–189.
16. Christensen ●B, Daniels TE, Maibach HI. Expression of OKT-6 antigen by Langerhans cells in allergic and non-allergic patch test reactions: Is the allergic response specific? Submitted 1984.
17. Friedmann PS. Disappearance of epidermal Langerhans cells during PUVA therapy. Br J Dermatol 1983; 105: 219–221.
18. Juhlin K, Shelley WB. Giant Langerhans cells induced by psoralen and ultraviolet radiation. Arch Dermatol Res 1979; 266: 311–314.
19. Tjernlund U, Juhlin L. Effect of UV-irradiation on immunological and histochemical markers of Langerhans cells in normal appearing skin of psoriatic patients. Arch Dermatol Res 1982; 272: 171–176.