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Ultraviolet therapy in lupus

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This review examines the use of ultraviolet (UV) therapy in lupus erythematosus (LE), a disorder usually associated with abnormally increased photosensitivity. In addition to the abnormal cutaneous response to ultraviolet radiation (UVR) exposure, photo-aggravation of systemic disease activity in systemic LE (SLE) may also occur. However, courses of UVR exposure may also be used in the treatment or prophylaxis of various photodermatoses, and LE now appears to be included in that group. Thus, several studies have reported apparent benefits of phototherapy in both cutaneous and systemic LE, although the underlying mechanisms remain obscure and final confirmation of such efficacy is still awaited in continuing studies. Lupus (2001) 10, 185–187.

Keywords: phototherapy; photopheresis; cutaneous lupus; systemic lupus erythematosus

Introduction

This review examines the use of ultraviolet (UV) therapy in lupus erythematosus (LE), a disorder usually associated with abnormally increased photosensitivity.1 In addition to the abnormal cutaneous response to ultraviolet radiation (UVR) exposure, photo-aggravation of systemic disease activity in systemic LE may also occur.2,3 However, courses of UVR exposure may also be used in the treatment or prophylaxis of various photodermatoses, and LE now appears to be included in that group. Thus, several studies have reported apparent benefits of phototherapy in both cutaneous and systemic LE, although the underlying mechanisms remain obscure and final confirmation of such efficacy is still awaited in continuing studies.

Ultraviolet radiation

The UV part of the electromagnetic spectrum comprises those wavelengths between 100 and 400 nm and the visible spectrum those between 400 and 800 nm (Figure 1). UVR comprises UVA (315–400 nm) and UVB (280–315 nm, the ‘sunburn’ wavelengths), while UVA has been subdivided into the longer ‘UVA1’ wavelengths (340–400 nm) and the shorter ‘UVA2’ (315–340 nm). UVA1 has so far appeared to demonstrate the greatest efficacy in the treatment of lupus, in contrast to UVA2, which is considered likely to share the lupus-aggravating properties of UVB.4 UVC (less than 280 nm) does not reach the earth’s surface because it is entirely absorbed by the ozone layer. UVR at the earth’s surface is therefore composed mainly of UVA (90–95%) and UVB.

Photosensitivity in LE

The specific definition and manifestations of abnormal photosensitivity in LE have been reviewed recently.1 A patient history of cutaneous photosensitivity has been reported in 57%5 to 73%2 of SLE patients, while several studies suggest that such photosensitivity is commoner in fairer skin types.2,6,7 Further, the most photosensitive major subset of cutaneous LE is subacute cutaneous LE (SCLE), in which 70–90% of patients are abnormally photosensitive by the American College of Rheumatology definition,8,9 while photosensitivity by the same criteria is estimated to occur in 50% of patients with discoid LE.10 Indeed, a fatality from a previously undiagnosed autoimmune disease has been reported in a psoriatic patient treated with psoralen photopheresis (PUVA).11 although PUVA does not significantly induce anti-nuclear antibodies (ANA) in otherwise healthy psoriatics.12

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In order to examine the wavelengths responsible for exacerbating LE, numerous cutaneous phototesting studies have been carried out, with various equipment and methods, but no clear LE-specific UV response has emerged; these studies have confirmed the clinical impression that the action spectrum for the photoprovocation of cutaneous LE is variable, but includes the UVB, UVA and occasionally visible light ranges. In addition to these rays from sunlight, sensitivity to the emissions from fluorescent tubes and photocopiers, although rare, has been reported in LE; these light sources produce mainly visible light.

### Phototherapy for lupus

Phototherapy for patients with LE has generally been considered contra-indicated because of the exacerbating effects of UVR. Thus, the suggestion that UVR exposure (UVA in particular) might be used as a therapy has been seen as particularly interesting. Several publications, including in particular a randomized controlled trial, have reported apparent significant therapeutic benefits from phototherapy in both the cutaneous and systemic forms of LE.

#### Experimental evidence of efficacy

In 1987, McGrath et al irradiated 20 New Zealand (NZB×NZW F1) lupus-prone mice with UVA and compared their survival to unirradiated controls. Mice were irradiated with 3.5 J/cm² UVA five times a week for 22 weeks. All exposed mice survived to 32 weeks, compared with 12 of 20 controls (P = 0.0013); the former group also demonstrated significantly lower levels of anti-DNA antibodies.

In later studies on human SLE patients, thoroughly reviewed recently, McGrath et al reported a significant reduction in disease activity indices, therapeutic drug use and anti-dsDNA titres after a 3 week course of UVA1, given at a low dose (60 kJ/m²/day) for five days a week. Therapy with visible light had no significant effect. The same group also reported a long-term benefit of UVA1 therapy in six patients with SLE, who were treated with one or two irradiations per week for several years, while a single case of SCLE has also been reported to improve significantly after a nine week course of UVA1. These studies and reports thus suggest that UVA1 phototherapy may be both effective and relatively safe, although the parameters studied have been to some extent subjective; in addition, the long-term risks for skin photocarcinogenesis and photoageing are at best uncertain, which suggests that it should be used only after other simpler treatments have failed.

#### Possible mechanisms of action

As with most other forms of phototherapy, the mechanism of any action of UVA in autoimmune skin disease is unknown. However, several recent reviews have claimed that UVA photons may promote DNA repair, cell-mediated immunity and apoptosis in as yet undemonstrated ways which may be responsible for any therapeutic applications.

### Photopheresis

Photopheresis involves the treatment of extracorporeal white blood cells with UVR exposure, after the patient has ingested a photosensitising dose of psoralen. Also known as extracorporeal photochemotherapy, the first stage requires venous access to remove whole blood; secondly, the white cells (buffy coat) are separated out and irradiated with UVA, after which the treated cells are finally re-infused. Lymphocytes treated by this process are significantly less responsive and have much shorter survival times than normal cells, which may explain why photopheresis has demonstrated efficacy in several T lymphocyte mediated diseases such as cutaneous T cell lymphoma (CTCL).

Knobler et al examined the use of photopheresis in an uncontrolled pilot study of 10 SLE patients; eight completed the trial, which involved photopheresis on two consecutive days each month for 6 months and then on alternate months for a further 6 months. SLE disease activity scores significantly improved in seven of the eight and few side effects were reported. More...
recently, Richter et al reported a patient with severe discoid LE who responded to treatment with photopheresis, in contrast to the effect of UVA1 therapy which appears instead to exacerbate discoid LE.

Thus, photopheresis inhibits lymphocyte function and has been used with some effect in the treatment of T lymphocyte-mediated diseases, while a degree of efficacy has also been reported in early therapeutic studies in SLE patients. However, neither UVA1 nor photopheresis are widely used as yet for the treatment of LE.

Clearly, further studies on these modalities of treatment are now needed. In that there is some therapeutic rationale, such studies are indeed justified. However, since LE is such a potentially serious disease and may be exacerbated by UVR exposure, combined with the unknown long-term side effects of UVA1, these studies should be conducted carefully and rigorously.

References