Inflammation in human skin induced by ultraviolet irradiation

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Summary

Pharmacologically active mediators of inflammation were obtained from suction bullae raised on normal and ultraviolet B (290-320 nm) inflamed human abdominal skin. The exudates obtained from the bullae were examined by superfusion cascade bioassay, by radioimmunoassay for $\text{PGF}_{2\alpha}$ and by column, thin-layer and gas-liquid chromatography.

Ultraviolet B (u.v.-B) irradiation of human skin produced an erythema which appeared after 2 hr, increased in severity up to 24 hr and persisted for more than 48 hr. Bioassayable and radioimmunoassayable prostaglandin activity was elevated at 6 hr, was maximal at 24 hr and had returned to normal by 48 hr. Topical application of indomethacin suppressed both the erythema and the increased concentration of $\text{PGF}_{2\alpha}$ as measured by radioimmunoassay. Chromatographic studies confirmed increased prostaglandin activity at 6 and 24 hr and in addition demonstrated an increase in arachidonic acid-like activity.

The results suggest that prostaglandins may play an important role between 6 and 24 hr of u.v.-B-induced erythema. Whether the reduction of erythema by indomethacin can be partially or wholly attributable to inhibition of prostaglandin biosynthesis is uncertain.

Introduction

The mechanisms by which ultraviolet radiation (u.v.r.) causes erythema is unknown. One possibility is that u.v.r. erythema is mediated by one or more vasoactive substances which act on the skin vasculature. This type of erythema may be suppressed by non-steroidal anti-inflammatory drugs, such as aspirin and indomethacin (Miller, Ruderman and Smith, 1967; Snyder and Eaglstein, 1974), which are known prostaglandin synthetase inhibitors. In addition, Sondergaard and Greaves (1970) have implicated prostaglandins as possible mediators in u.v.-B-induced erythema.

It was therefore of interest to study prostaglandin-like activity in human skin at various intervals following u.v.-B irradiation.

Materials and methods

Two areas of clinically normal abdominal skin of thirty-three adult volunteers was irradiated with three times the minimal erythema dose (3 MED) of u.v.-B (290-320 nm) using four FS 20 Westinghouse sun tubes, having an intensity of $430 \mu\text{Wcm}^{-2}$ at 30 cm. Immediately after irradiation 2.5% indomethacin was applied to one irradiated area at a dosage of $3 \mu\text{l cm}^{-2}$. The degree of erythema was assessed visually. Exudate was collected, at 6, 24 and 48 hr after irradiation, from irradiated and control non-irradiated skin by a suction bullae technique (Black *et al.*, 1976). The exudates were examined for smooth muscle contracting activity by superfusion cascade bioassay (Vane, 1964) and for $\text{PGF}_{2\alpha}$ by radioimmunoassay. Ethyl acetate extractable fractions from the exudates were examined for various prostaglandins and related compounds by Lipidex 5000 gel partition, thin-layer and gas-liquid chromatography as previously described by Plummer *et al.* (1977).

Results

Irradiation of human abdominal skin produced erythema in all subjects studied. The erythema appeared at 2 hr, was maximal at 24 hr and persisted for more than 48 hr. Topical indomethacin partially suppressed the erythema seen at 24 hr. Prostaglandin-like activity was detected by bioassay in exudate from normal non-irradiated skin. At 6 and 24 hr after irradiation the concentrations of prostaglandin-like activity were significantly increased. However, at 48 hr the concentration was not significantly different from that of the control (Table 1). Similarly, radioimmunoassayable $\text{PGF}_{2\alpha}$ was significantly elevated at 24 hr. Initial studies indicate that the concentrations of immunoassayable $\text{PGF}_{2\alpha}$ seen 24 hr after u.v.-B irradiation were prevented by topical application of indomethacin (Table 1).

Chromatographic studies suggest that u.v.-B

TABLE 1. Concentrations of prostaglandin-like activity in exudate from human skin at 6, 24 and 48 hr after u.v.-B irradiation and the effect of indomethacin on PGF_{2α} at 24 hr after irradiation

Method	Compound	Control	Time after irradiation (hr)			
			6	24	24+ (Indomethacin)	48
Bioassay	PG-like* ng/ml	31.3 ± 12.6 n=10	100 ± 17.7 n=4 P < 0.02	243.8 ± 90.4 n=4 P < 0.005		56.3 ± 19.4 n=4 P > 0.30
Radioimmunoassay	PGF _{2α} ng/ml	21.3 ± 4.8 n=27	43.8 ± 16.5 n=9 P > 0.10	56.7 ± 9.0 n=11 P < 0.0005	11.3 ± 5.6 n=9 P > 0.5	22.7 ± 4.7 n=8 P > 0.40

* Measured as PGE₂ equivalents.

irradiation increases the concentration of arachidonic acid, PGE₂ and PGF_{2α} at 6 and 24 hr after irradiation. Likewise, these techniques failed to provide evidence of elevated prostaglandins at 48 hr when the erythema was still present.

Discussion

The present study provides evidence of a rise in human skin prostaglandin and arachidonic acid-like activity at 6 and 24 hr after u.v.-B irradiation when erythema is developing. However, at 48 hr, when the erythema is still maximal, the levels of prostaglandins and arachidonic acid-like activity were not significantly different from the controls. These findings raise the possibility that prostaglandins may be important mediators of inflammation at 6 and 24 hr after u.v.-B irradiation, since the erythema and prostaglandins are suppressed by indomethacin. However, other mediator(s) may be important at 48 hr, or the erythema seen at 48 hr could result not from increased blood flow but to a pooling of blood in the skin. Alternatively, the increased prostaglandin activity in u.v.-B-induced inflammation may be unrelated to the concomitant development of redness; the suppressive effect of indomethacin on u.v.-B erythema being attributable to actions of indomethacin other than its ability to suppress prostaglandin synthesis. Studies of the

quantitative relationships between changes in concentrations of prostaglandins and related compounds, other non-prostaglandin mediators and blood flow in irradiated skin are needed.

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