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Effects of ultraviolet light on the tension of isolated human cavernosal smooth muscle from non-diabetic and diabetic impotent men

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Abstract The effects of ultraviolet (UV) light (310 nm) on human cavernosal smooth muscles were investigated. Cavernosal strips were obtained from men during penile prosthetic surgery. When the cavernosal strips were irradiated with UV light in an organ bath, after precontraction by norepinephrine (100 nM) for 10, 20, 40 and 90 s at intervals of 3 min, the contracted cavernosal smooth muscles from the impotent men without vascular risk factors (controls) showed relaxation depending on the duration of irradiation. However, the relaxation was not found when the strips were pretreated with methylene blue (10 μM) or their epithelia were denuded. The relaxation response of the cavernosal strips from the patients with diabetogenic impotence was significantly reduced compared with that of the controls. Photorelaxation of human cavernosal strips therefore seems to be dependent on endothelium.

Key words Ultraviolet light · Cavernosal smooth muscle · Diabetogenic impotence · Photorelaxation

Introduction

Since Furchgott et al. [5] reported ultraviolet (UV) light-induced vasorelaxation in the rabbit thoracic aorta in 1955, it has been suggested that the UV-induced vasorelaxation in the vascular preparation may be associated with cyclic GMP accumulation in the tissue through activation of soluble guanylate cyclase by UV irradiation. This is mostly based on the indirect evidence that the UV-induced vasorelaxation, like endothelium-dependent relaxation, is inhibited by guanylate cyclase inhibitors such as hemoglobin and methylene blue, and potentiated by a guanylate cyclase activator, NaNO [2, 6, 13]. The responses to the UV irradiation could be different according to animal species. Furchgott et al. [6–8] described relaxation of endothelium-denuded strips on exposure to light. Ryu et al. [15] reported that the endothelium-intact preparations responded to UV irradiation with contraction depending on the duration of irradiation, whereas a very sensitive relaxation response was observed in the endothelium-removed one. We could not find any reports of a photo-induced response of cavernosal smooth muscles, and this study therefore investigated the effect of UV light on isolated human cavernosal smooth muscles.

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Materials and methods

Cavernosal tissues were obtained during penile prosthetic surgery in 16 impotent men (mean age 46.88 ± 12.95 years) with no vascular risk factors (diabetes mellitus, hyperlipidemia, smoking, hypertension, obesity, heart problems, etc.) and five impotent men (mean age 52.75 ± 11.96 years) with diabetes mellitus. The duration of diabetes was 12.23 ± 4.57 years and the type of diabetes was insulin dependent. The cavernosal tissues were dissected into strip preparations, measuring approximately 2 × 2 × 6 mm, and mounted under approximately 1 g resting tension in 30-ml organ bath chambers containing Krebs bicarbonate solutions at 37 °C gassed with 95% O_2 and 5% CO_2. One end of the cavernosal strip was fixed at the bottom of the bath and the other end connected to the force displacement transducer (Havard Apparatus). Composition of the Krebs bicarbonate solutions (in mM) was NaCl 118.3, KCl 4.7, $CaCl_2$ 2.6, $NaHCO_3$ 26, $MgCl_2$ 1.2, $NaHPO_4$ 1.2, glucose 11.1.

After strip tension was stabilized, the relaxation and contractile capacity of the strips were pretested by exposure to high concentrations of norepinephrine and acetylcholine. When the stable tension level of the strip was reached, norepinephrine bitartrate (100 nM) (Sigma) was added to the organ bath and the change in contractility of the strip was recorded on a recorder (Universal Oscillograph, Havard Apparatus).

In tension experiments, a UV lamp (UVL-56; peak wavelength 366 nm, intensity 18.4 W, UVP) was placed at a distance of 1.5 cm from the strips, and long-wave UV light (310 nm) was irradiated on to the strips in the presence of intact endothelium for 10, 20, 40 and

90 s at intervals of 3 min in the dark-room with a 5-W red lamp. The relaxation responses to the UV light of the impotent patients without vascular risk factors (controls, $n = 16$) were compared with those with diabetes mellitus ($n = 5$). The experiments were then repeated using endothelium-intact cavernosal strips from the impotent patients without vascular risk factors which were pretreated with methylene blue (10 μM, $n = 5$) 10 min before application of norepinephrine and using endothelium-denuded strips ($n = 5$) by rubbing. The experimental data were analyzed and compared using Student's t-test.

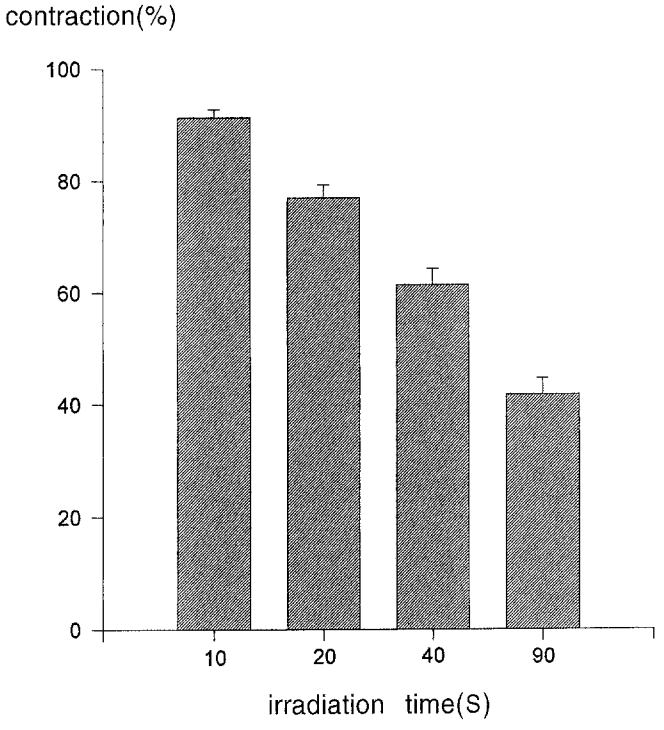

Fig. 1 Ultraviolet irradiation (310 nm) produces relaxation of the endothelium-intact cavernosal strips ($n = 16$) from impotent patients without vascular risk factors, which were precontracted with norepinephrine (100 nM), depending on the duration of irradiation. The relaxation response was disappeared immediately when the UV irradiation was stopped

Results

The endothelium-intact cavernosal strips from the impotent patients without vascular risk factors (controls), which were precontracted with norepinephrine (100 nM), showed reversible relaxation depending on the duration of irradiation (Fig. 1). The same results were also obtained with the various concentrations of norepinephrine (from 1 nM to 0.1 mM). However, no relaxation was noted regardless of duration of irradiation, when the strips were denuded or the endothelium-intact cavernosal strips were pretreated with methylene blue (Fig. 2). When the denuded strips were sandwiched with strips of intact endothelium, the relaxation responses appeared again depending on the duration of irradiation. However, the photorelaxation was not noted after removal of the sandwiched strips of intact endothelium (Fig. 3). The relaxation response of the cavernosal strips from the patients with diabetogenic impotence was significantly reduced compared with that of the controls ($P < 0.05$) (Fig. 4).

Discussion

It has been reported that UV light induces relaxation of strips of rabbit thoracic aorta [5, 7, 8, 16]. This response was similar to endothelium-dependent relaxation as it was inhibited by hemoglobin and methylene blue, and was accompanied by an increase in cyclic GMP in the smooth muscle [7–9]. It has been suggested that the photo-induced factor responsible for this effect has properties similar to endothelium-derived relaxing factor and NO [4]. Venturini et al. [16] suggested that the existence of a fine NO-yielding photosensitive store of nitrosylated compound(s) might contribute to the control of vascular tone. The wavelength of light which elicited maximal relaxation was 310 nm [6].

UV-light-induced relaxation response in arterial smooth muscles was also reported in rat thoracic aorta

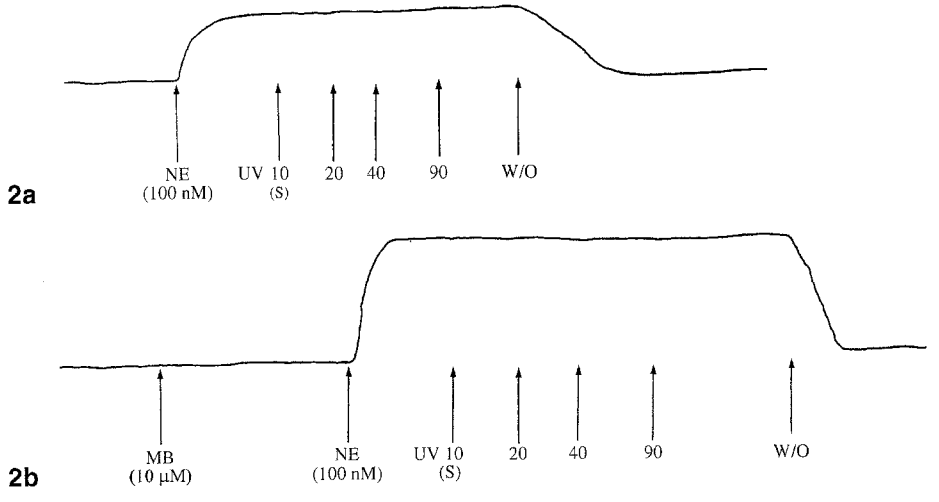

Fig. 2a,b Relaxation of the cavernosal strip from an impotent patient without vascular risk factor is not found regardless of the duration of irradiation when the strip was denuded (**a**) or pretreated with methylene blue (**b**)

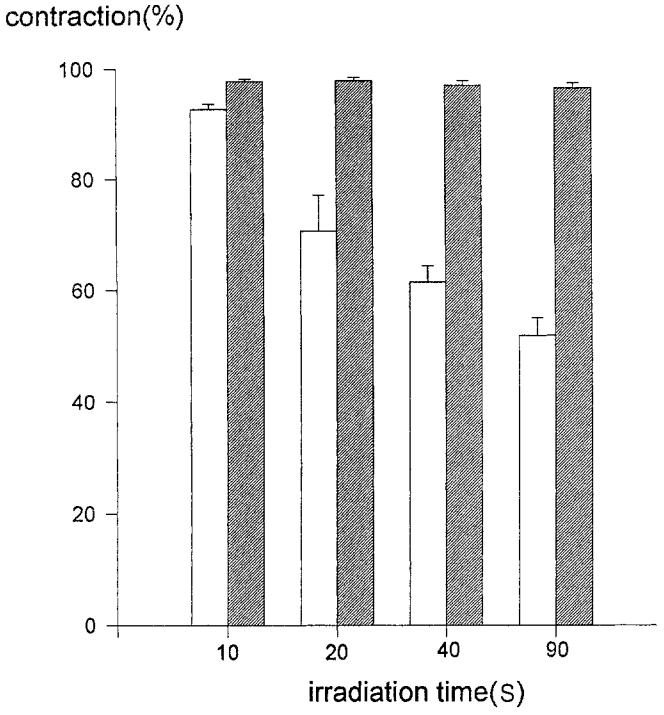

Fig. 3 Denuded strips sandwiched with a strip of intact endothelium show relaxation again depending on the duration of irradiation (□), but the photorelaxation does not appear after removal of the sandwiched strips of intact endothelium regardless of the duration of irradiation ▨

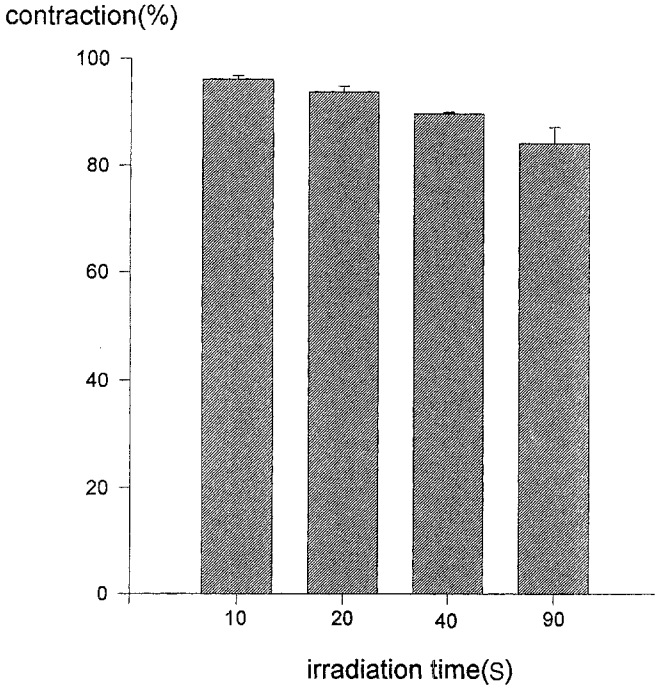

Fig. 4 Relaxation response of cavernosal strips ($n = 5$) from patients with diabetogenic impotence is significantly reduced compared with that of controls (Fig. 1)

[12, 14], bovine mesenteric artery [9, 10], porcine cerebral artery [1], and dog coronary artery [6]. There may be differences in the responses to UV irradiation according to the animal species and the tissues employed even in the same animal [3]. Ryu et al. [15] reported that endothelium-intact preparations of the isolated rat thoracic aorta precontracted with phenylephrine responded to UV irradiation with further contraction depending on the duration of irradiation, whereas a very sensitive relaxation response was observed in the endothelium-removed ones. Baik et al. [2] reported that the magnitudes of the photo-induced relaxation in rabbit thoracic aortae and porcine coronary arteries were not significantly different in either the endothelium-intact rings or the endothelium-denuded rings. In our study, the cavernosal strips of the impotent patients without vascular risk factors, which were precontracted by norepinephrine, showed radiation time-dependent relaxation. When their epithelia were denuded, however, the cavernosal smooth muscles showed no relaxation responses, which appeared again when the denuded strip was sandwiched with endothelium-intact strip. We found in another study that relaxation of the isolated cavernosal smooth muscle to endothelium-independent vasodilators was similar in nondiabetic and diabetic men with impotence, but the relaxation response of the tissues to endothelium-dependent vasodilators was significantly reduced in the diabetic group compared with that in the nondiabetic group [11]. In this study, the relaxation response of the cavernosal strips from the diabetic patients with impotence to UV light was significantly reduced compared with that of the controls. All these findings are suggestive of endothelium-dependent photorelaxation of the human cavernosal smooth muscle. And the finding that both the denuded strips and the endothelium-intact strips pretreated with methylene blue showed no photorelaxation suggests the relaxation response of human cavernosal smooth muscle might be due to the inhibition of guanylate cyclase.

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