

Minimal Erythema Dose (MED) in Normal Canine Skin by Irradiation of Narrow-Band Ultraviolet B (NB-UVB)

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ABSTRACT. Narrow-band UVB (NB-UVB) is light over a very narrow band of wavelengths (around 311 nm) that is concentrated in the therapeutic range and minimally in the sunburn range. It has therefore become the phototherapy treatment of choice for skin diseases. The minimal erythema dose (MED) on canine skin for standardizing dosage schedules in NB-UVB treatment and histopathological analyses were performed in these dogs. In all 32 dogs tested, the MED ranged from 432 to 864 mJ/cm². There were no significant differences in MED among breeds, sex and age groups. Histopathology obtained from areas irradiated by MED showed only mild vascular dilatation. These findings might be valuable for the application of NB-UVB phototherapy to canine skin diseases.

KEY WORDS: dog, minimal erythema dose, narrow band ultraviolet B, phototherapy.

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Ultraviolet (UV) is invisible light that is part of the energy that comes from the sun [1]. It is made up of three types of rays from the longest wavelength to the shortest: UVA, UVB and UVC. Prolonged exposure to the sun causes skin damage and sometimes skin cancer because of these UV rays. However, scientists have found that although the different wavelengths of light can have adverse effects, they can also be used as UV phototherapy to treat skin diseases [6, 13]. UV phototherapy is exposure to intense UV light sources of a specific wavelength or narrow range of wavelengths for specified amounts of time to treat a variety of skin disorders [14, 17]. In human medicine, UVA and UVB irradiation has been used successfully to treat a number of diseases, including psoriasis, cutaneous T-cell lymphoma and atopic dermatitis [10, 15, 16, 18].

In human medicine, phototherapy devices use either short-wavelength broad-band UVB rays or the long rays of UVA. Broad-band UVB bulbs emit light in a broad range that includes the therapeutic wavelengths specific to the treatment of skin disorders but also is responsible for causing sunburn, which increases the risk of skin cancer. This limits the usefulness of therapeutic broad-band UVB [1]. In contrast, narrow-band UVB (NB-UVB) emits light over a very short range of wavelengths concentrated primarily in the therapeutic range [9]. In addition, NB-UVB phototherapy induces apoptosis of dermal T lymphocytes [12]. Thus, NB-UVB is considered effective for controlling human T-cell-mediated skin diseases such as cutaneous T cell

lymphoma or atopic dermatitis [3, 7, 8, 11].

The minimal erythema dose (MED) is the minimum dose of radiation that produces perceptible skin erythema, and it is expressed in Joules per square centimeter (J/cm²). The MED must be determined before UV therapy in order to minimize the inflammation of irradiated skin and define the initial irradiation dosage. However, in veterinary medicine, few studies have been published on the effects of the specific band of UV on canine skin. Our aims in this study were to determine the MEDs on normal canine skin in order to standardize dosage schedules in NB-UVB treatment and to determine whether MEDs vary with canine breed, gender, and age. Moreover, to confirm the effect of NB-UVB on dog skin more precisely, histopathological analyses were performed in 11 dogs.

Thirty-two dogs (20 males and 12 females; median age 6 years, range 1–11 years) without skin lesion were enrolled in the study. This study was approved by the Committee of Experimental Animals of Tokyo University of Agriculture and Technology. The dogs' abdominal hair was clipped with an electric clipper 3 days before NB-UVB irradiation. A UVB lamp (Philips TL-01, Daavlin, CA, U.S.A.) with a peak emission of 311 nm was used. The dosage of irradiation by narrow-band UVB depends on the exposure time and the distance between the lamp and the irradiated skin. Each dog had an aluminum foil template with an aperture (10 mm square) applied to the skin of its abdomen. The remainder of the dog's skin was covered with sheets to prevent exposure to the NB-UVB. Every effort was made to maintain a distance of exactly 2 cm between the NB-UVB source and the irradiated skin surface. A 10-min warm-up time was strictly observed. The abdominal skin of each dog was exposed to 6 graded doses of NB-UVB, from 54 to 864 mJ/cm² (54, 108, 216, 432, 648 and 864 mJ/cm²). In human medicine, the MED is defined as the smallest dose of radiation to result in just detectable erythema, as assessed

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visually 24 hr after irradiation. We used the same definition for the MED on dog skin. Furthermore, biopsy specimens were obtained under local anesthesia with 5% xylocaine and medetomidine from the un-irradiated area of abdominal skin, the MED area, and the areas irradiated with one dose below and above the MED.

In all 32 dogs tested, erythema was recognized on skin irradiated with 432 mJ/cm² or more but not on that irradiated with 216 mJ/cm² or less. The MED therefore ranged from 432 to 864 mJ/cm², and in 20 out of 32 (62.5%) dogs, the MED was 648 mJ/cm² (Fig. 1). The MED was separated into three groups according to breed, namely beagles, shi-tzus and

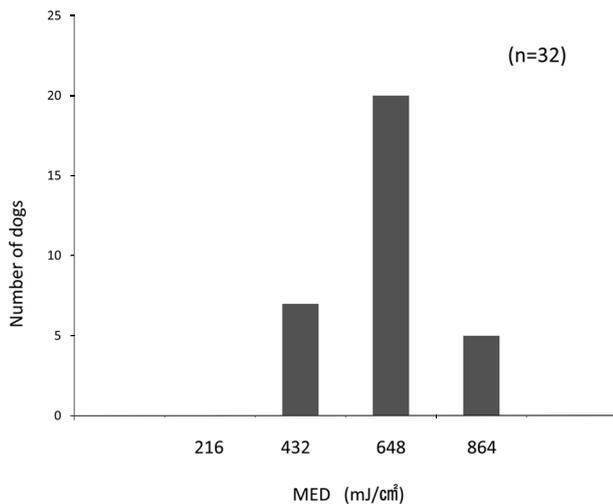


Fig. 1. All 32 dogs showed erythema on the skin irradiated by more than 432 mJ/cm² of NB-UVB. MED (minimum erythema dose) range was from 432 to 864 mJ/cm². The irradiation of NB-UVB at 432 mJ/cm² caused erythema in five dogs out of 32 dogs. At 648 mJ/cm² of irradiation, 20 out of 32 dogs showed erythema on the skin, whereas seven dogs out of 32 dogs did not show erythema until 864 mJ/cm².

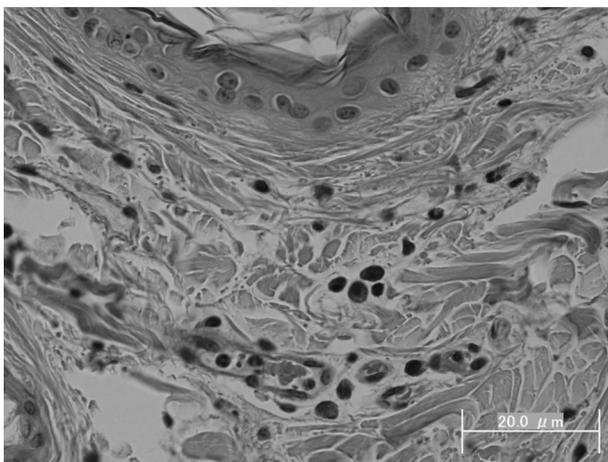


Fig. 2. Histopathology of the skin obtained from the area where irradiated 648 mJ/m² of narrow band ultra violet B (NB-UVB). There are no abnormal findings in epidermis and dermis except the dilatation of capillary vessels (Hematoxyline and eosin).

mongrels. Differences among breeds were analyzed statistically by using one-factor ANOVA. In the 5 beagles (MED range, 432–648 mJ/cm²), 11 shi-tzus (range, 648–864 mJ/cm²) and 6 mongrels (range, 432–864 mJ/cm²) tested, there were no significant differences in MED among breeds. As MED does not change with gender in humans [2], we evaluated whether MED varied between male and female dogs. Differences among the 22 males (range, 432–864 mJ/cm²) and 12 females (range, 432–864 mJ/cm²) were analyzed statistically by using the Mann-Whitney U test. As a result, there were no significant differences in MED between male and female dogs. The difference in age of MED is not significant in humans [4]. Range of ages in dogs used in this study was 1 to 11 years. The relationship between MED and age was analyzed statistically by using the Spearman's rank test. There was no significant correlation between MED and age in dogs. These findings together suggest that the MED does not vary by dog breed, gender or age.

To further examine the safety of NB-UVB irradiation of canine skin, histopathological analysis of irradiated skin was performed in four dogs. Biopsy specimens were obtained from un-irradiated skin, skin irradiated with one dose below the MED, skin irradiated with the MED and skin irradiated with one dose above the MED by a biopsy trepan under the general anesthesia. Sections were stained with hematoxylin and eosin to evaluate NB-UVB-induced epidermal damage and dermal inflammation. All areas irradiated with the MED showed mild vascular dilatation in the dermis and no significant change in epidermal cells (Fig. 2). In addition, perivascular infiltration of mononuclear cells was recognized in the superficial dermis in areas irradiated with the MED or higher doses, and the change was more notable in areas irradiated with one dose above the MED. There were no apparent degenerative changes in any areas tested. Even though each dog had received different Joules of MED, the histopathological observations were similar in all 11 dogs tested. No pathological changes were found in the control

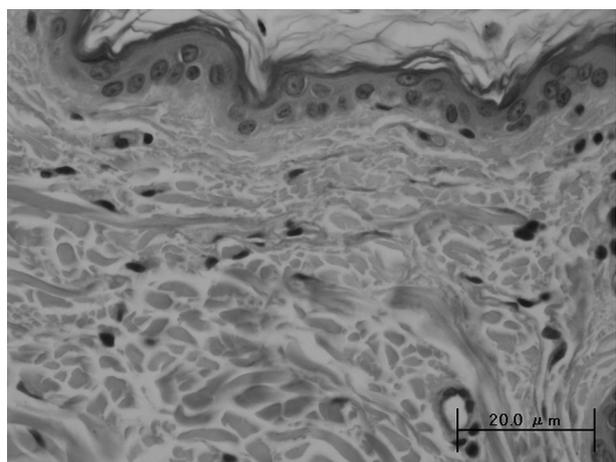


Fig. 3. Histopathology of the skin from normal dogs revealed no apparent dilatation of capillary vessels and a few infiltrates (Hematoxyline and eosin).

areas (Fig. 3). These findings suggest that MED irradiation with NB-UVB might be safely applied to canine skin. In our study, the average MED in dogs, and the resultant histopathological findings, were approximately consistent with those in humans, even though dogs have thinner skin [5]. Furthermore, the results of the statistical analysis indicated that the MED did not vary with the breed, gender, or age. To our knowledge, there have been no previous studies examining the MED of narrow-band UVB in dogs. These observations should provide baseline MED data and will be valuable in future applications of NB-UVB phototherapy in veterinary dermatology.

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