経表皮水分蒸散量(TEWL)の上昇は犬の皮膚バリア機能破壊を反映する

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Transepidermal Water Loss (TEWL) Reflects Skin Barrier Function of Dog

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ABSTRACT. The correlation between skin barrier function and transepidermal water loss (TEWL) was evaluated in dogs. Stratum corneum (SC) of 10 healthy dogs was removed by tape stripping (TS), which decreased the corneal layer to allow for permeation of fluorescent dye into skin. TEWL of damaged skin was measured with the closed-chamber-type TEWL analyzer, CC-01. The frequency of TS was directly related to the decrease of SC and the increased permeation of fluorescent dye, and TEWL increased with increasing impairment of skin barrier function. The results suggest that increased TEWL reflects impaired canine skin barrier function.

KEY WORDS: canine skin, skin barrier function, transepidermal water loss.

The skin functions as an interactive wall of mammalian body, controlling egress of water and suppressing ingress of environmental and microbial agents, thereby preventing skin diseases [3]. Therefore, the maintenance of skin barrier function is critical for the treatment of skin diseases in mammals.

Transepidermal water loss (TEWL) is defined as the volume of water that passes from inside to outside of the body through the epidermal layer. TEWL measurement has been used to evaluate skin barrier function in human [1, 5, 8], and an increase in TEWL has been reported to reflect impairment of skin barrier function [2], i.e., high TEWL suggests low skin barrier function. In addition, in human, a number of studies have suggested that high TEWL is associated in various skin diseases, including atopic dermatitis, psoriasis, contact dermatitis, and ichthyosis [4, 10, 11, 14]. Thus, TEWL is thought to be a useful parameter that characterizes skin barrier function in human.

Many skin disorders are suggested to be associated with skin barrier function in dogs [7]. However, the relationship between skin disease and the barrier function is not well analyzed because of paucity of studies on the TEWL value in normal and damaged canine skin. In this study, we evaluated whether TEWL could reflect impaired canine skin barrier function or not.

Ten healthy dogs (8 crossbred dogs and 2 beagles, age range 7–13 years, 1 female, 3 sterilized females, and 4 neutered males) were enrolled in this study. All animals were fed on the same food and kept in an air-conditioned room. Two different anatomical areas, lumbar skin and inguinal skin, were used for TEWL measurement. Hair on both areas of each dog was clipped before measurement. Measurements were performed at 23–25°C and 45–65% relative humidity. All dogs were acclimated at least 30 min to the measurement conditions. All experiments were performed in accordance with the guidelines of animal research committee in Tokyo University of Agriculture and Technology.

Tape stripping (TS) is a well-known method to artificially damage the stratum corneum (SC) [9, 12]. TS was performed on the left and right sides of lumbar skin and inguinal skin of five of ten dogs, using adhesive cellophane tape (Nichiban, Tokyo, Japan). The tape-stripped areas were divided into five parts, and skin of each part was tape-stripped 0, 5, 10, 15 or 20 times, respectively. After TS, TEWL in each area was measured three times with a closed-chamber-type TEWL analyzer (CC-01, Kao Corporation, Japan) [15]. TEWL was expressed as mean ± SD.

Skin was sampled from each of the five tape-stripped areas with 6 mm biopsy trepan. Then, fluorescent dye was applied to tape-stripped areas of the other 5 dogs in order to visualize skin damage. Fluorescence dye (10%, Alcon, Japan) was measured 0.05 ml and poured into the paper disc and held to the skin by Finn chamber (Epitext, Helsinki, Finland). Thirty min after application, the patch test area was washed with physiological saline solution, and permeation of fluorescent dye into the skin was observed with Wood’s lamp in a darkroom.

Figure 1 shows the histopathological findings and percutaneous permeation of fluorescent dye into lumbar skin of a representative dog. The non-stripped area had more than 10 SCs, but after stripping 5 times, more than half of the SC was removed. Only a few SCs were left on the epidermis after stripping 10 times, and permeation of the fluorescent dye was apparently visible. Moreover, stripping 15 times completely removed the SC, and the extent of permeation of the fluorescent dye was the same as that of the area stripped 10 times. These findings indicate that similar to human skin, TS of canine skin impaired skin barrier function to allow for permeation of fluorescent dye into the skin.

Figure 2 shows the relationship between TEWL and frequency of tape stripping in 10 dogs. In the lumbar region,
Histopathological findings and permeation of fluorescent dye after tape stripping in lumbar skin. According to tape stripping frequency, canine skin stratum corneum gradually decreased and percutaneous permeation of fluorescent dye was accelerated. 0, non-stripped area. 5, 10, 15, and 20, frequency of tape stripping.

**Fig. 1.** Relationship between TEWL and frequency of tape stripping. TEWL is significantly increased in lumbar skin and inguinal skin when frequency of tape stripping was increased, compared with non-stripped area (One-factor ANOVA, $P<0.05$). There is a positive correlation between TEWL and frequency of TS in both areas (Spearman's rank correlation, $P<0.05$).

TEWL in non tape-stripped area was $20.59 \pm 5.51$ (g/m$^2$·hr), but after stripping five times, it increased to $28.17 \pm 7.47$ (g/m$^2$·hr). After stripping 10 times, it increased to $44.87 \pm 24.02$ (g/m$^2$·hr), and after stripping 15 times, it was $66.61 \pm 24.94$ (g/m$^2$·hr). TEWL was $87.58 \pm 30.59$ (g/m$^2$·hr) after stripping 20 times. In the inguinal region, TEWL in non tape-stripped area was $20.17 \pm 3.60$ (g/m$^2$·hr), but increased to $33.37 \pm 8.53$ (g/m$^2$·hr) after stripping 10 times. It was $63.94 \pm 19.78$ (g/m$^2$·hr) after stripping 15 times, and increased to $129.05 \pm 64.11$ (g/m$^2$·hr) after stripping 20 times. The mean TEWL values increased with the frequency of stripping and were significantly higher than those in the non-stripped area on both lumbar skin and inguinal skin (One-factor ANOVA, $P<0.05$). And also, there is a positive correlation between TEWL and frequency of TS in both areas (Spearman's rank correlation, $P<0.05$).

The purpose of this study is to evaluate the relationship between TEWL and impaired skin in dogs. There are some studies of TEWL in canine skin, but most of them used open-chamber-type instruments [6–13]. We measured TEWL with a closed-chamber-type instrument, which is considered to be better than the open chamber type because it minimizes the effects of a relative humidity and movement of dogs [15].

We found that the increased frequency of tape stripping induced high TEWL value. Mean TEWL was higher in the area stripped 10 times than in the non-stripped area, and fluorescent dye permeated into the skin as the SC was damaged. Since fluorescent dye does not permeate into the skin when skin barrier function is intact, as observed in the non-stripped area, the permeation of fluorescent dye is an indication that skin barrier function was impaired. Taken together, it is conceived that TEWL and impairment of skin barrier function may have a positive correlation.

In conclusion, the relationship between TEWL and damaged skin in dogs was clarified. TEWL measurement enables us to evaluate canine skin barrier function quantitatively. The advantages presented by this non-invasive procedure, quantifying of skin barrier state will give us new insights into skin biology and the pathogenesis and treatment of skin diseases.
REFERENCES