A-4.1 Epidemiological studies on the health effects of ultraviolet sun exposure in humans

Contact person Naohito Yamaguchi
Chief, Cancer Information and Epidemiology Division
National Cancer Center Research Institute
Ministry of Health and Welfare
5-1-1 Tsukiji, Chuo-ku 104-0045 Japan
Tel: +81-3-3542-2511 Fax: +81-3-3546-0630
E-mail: nyamaguc@gan2.ncc.go.jp

Total Budget for FY1996-1998 60,740,000 Yen (FY1998; 24,762,000 Yen)

Abstract The mortality and morbidity of skin malignancies and their precursor lesions were studied in relation to the ultraviolet exposure. The prevalence of solar keratosis was found to be higher in Ieson Okinawa, where the ultraviolet exposure is among the highest in Japan, as compared to Kasai city, Hyogo, with medium ultraviolet exposure. This suggests that the ultraviolet radiation in Japan can cause skin cancer, and further studies are needed for the prevention of skin cancers due to ozone depletion. The mortality rate of skin malignancies was found to be not a good indicator for the change in skin malignancies due to ozone depletion. A good system to monitor the incidence of skin cancers should be developed.

Key Words Solar keratosis, Skin cancer, Epidemiology, Ultraviolet

1. Introduction

The health effect of ultraviolet radiation is one of the most important health problems in Japan, since the knowledge on how the increase in exposure to ultraviolet radiation due to ozone depletion might give harmful health effects to Japanese is far from adequate. This project focuses on the risk of skin malignancies and their precancerous lesions as the health effects of UV radiation in relation to different exposure levels in different regions. Special dermatological surveys have also been conducted to evaluate the prevalence of solar keratosis in different lesions.

2. Research objective

This project aims at evaluating the risk of skin malignancies and precancerous lesions, using epidemiological methods. Specific objectives are;

(1) Epidemiological analyses of mortality due to skin cancers. Time trend analysis and geographical correlation analysis are conducted.
(2) Survey of prevalence of skin cancer and solar keratosis. Special dermatological surveys are conducted to estimate the prevalence and incidence rates of skin cancers

and precancerous lesions.

(3) Geographical correlation analysis of ultraviolet exposure and mortality of cancers other than skin cancer.

(4) Building a research protocol for case-control study of skin cancer.

3. Research Methods

(1) Epidemiological analyses of mortality due to skin cancers. For the time trend analysis, the age-specific mortality rates of malignant melanoma and non-melanoma skin cancer are analyzed for males and females separately. For the geographical correlation analysis, the country is divided into 11 regions, the ultraviolet B exposure levels are estimated for these regions, and then the correlations between UV-B exposure level and skin cancer mortality are analyzed for malignant melanoma and non-melanoma skin cancer separately.

(2) Survey of prevalence of skin cancer and solar keratosis. Two areas are selected for special dermatological surveys; Kasai city in Hyogo prefecture, where the ultraviolet exposure lies in the medium range and Ieson in Okinawa prefecture, where the ultraviolet exposure is among the highest. The dermatological surveys are conducted annually to estimate the prevalence and incidence rates of skin cancers and precancerous lesions.

(3) The standardized mortality ratios of various cancers other than skin cancer are analyzed in relation to the ultraviolet B exposure level in 11 different regions mentioned in (1).

(4) Building a research protocol for case-control study of skin cancer. The index for the cumulative lifetime exposure to ultraviolet radiation is investigated.

4. Results

(1) Epidemiological analyses of mortality due to skin cancers

As a result of time trend analysis of skin cancer mortality during the period 1975 to 1995, the malignant melanoma was found to increase during this period in both males and females. On the other hand, the mortality rate (per 100,000) from non-melanoma skin cancer was found to decrease from 3.5 in 1975 to 1.6 in 1995 among males, and from 2.8 in 1975 to 1.4 in 1975 among females, respectively.

The geographical correlation analysis for the mortality during the period 1983 to 1992 revealed that there was no significant correlation between estimated ultraviolet exposure level and skin cancer mortality measure by the standardized mortality ratio. This result suggested that the mortality rate may not be a good indicator for the skin cancer risk, in light of relatively good survival.

(2) Survey of prevalence of skin cancer and solar keratosis.

By the special dermatological surveys, the prevalence rate (per 100,000) of solar keratosis was estimated to be 281.5 and 120.4 in males and females of Kasai city, whereas that in Ieson was estimated to be 808.3 and 876.7 in males and females, respectively. The differences were statistically significant. Interestingly, the

prevalence of solar keratosis was found to correlate with the number of seborrheic keratoses. Furthermore, the prevalence of solar keratosis was found to be lower among sun-screen users than non-users.

(3) Geographical correlation analysis of cancers other than skin cancer.

The standardized mortality ratio for leukemia and uterine cancer showed positive geographical correlations with ultraviolet B exposure. Further studies are needed to investigate the biological relevance of this observation.

(4) Building a research protocol for case-control study of skin cancer.

The number of wrinkles and degree of pigmentation on the facial skin were investigated in relation to the cumulative lifetime exposure to ultraviolet radiation. As a result, the number of skin wrinkles was found to be a good indicator.

5. Discussion

In this study, the prevalence rate of solar keratosis in Ieson, Okinawa, was found to be four times as high as that in Kasai city, Hyogo. This finding suggests that the skin cancer in Japan could increase as a result of the increase in ultraviolet radiation. The correlations between the prevalence of solar keratosis and other skin factors such as skin types and the number of seborrheic keratosis indicate that the high risk group of sun-exposure related skin malignancies might be identifiable. Furthermore, the difference in the prevalence of solar keratosis between sun-screen users and non-users could give us a suggestion on the prevention of skin cancers in Japan.

In our study, the mortality rate of non-melanoma skin cancer was found to have decrease in the recent decades in Japan. This might suggest that other factors such as improved survival and change in diagnostic criteria should be taken into consideration. We should develop a systematic way to monitor the change in skin cancer incidence in Japan.

6. Publications

1) Ueda M, Ouhtit A, Bito T, Nakazawa K. Lubbe J, Ichihashi M, Yamasaki H, Nakazawa H: Evidence for UV-associated activaton of telomerase in human skin. Cancer Res 57: 370-374, 1997

2) Ahmed NU, Ueda M, Ichihashi M: p21WAF1/CIP1 expression in non-melanoma skin tumors. J Cutan Pathol 24: 223-227, 1997

3) Ahmed NU, Ueda M, Ichihashi M: Increased level of c-erbB-2/new/HER-2 protein in cutaneous squamous cell carcinoma. Br J Dermatol 136 (6):908-912, 1997

4) Ouhtit A, Ueda M, Nakazawa H, Ichihashi M, Dumaz N, Sarasin A, Yamasaki H: Quantitative detection of ultraviolet-specific p53 mutations in normal skin from Japanese patients. Cancer Epidemiology, Biomarkers & Prevention 6: 433-438, 1997

5) Funasaka Y, Ichihashi M: The effect of ultraviolet B induced adult T cell leukemia-derived factor/ thioredoxin (ADF/TRX) on survival and growth of human melanocytes. Pigment Cell Res 10: 68-73, 1997

6) Naruse K, Ueda M, Nagano T, Suzuki T, Harada S, Imaizumi K, Watanabe S, Ichihashi M: Prevalence of actinic keratosis in Japan. J Dermatol Sci 15(3); 183-187, 1997

7) Ahmed NU, Ueda M, Ito A, Ohashi A, Funasaka Y, Ichihashi M: Expression of fibroblast growth factor receptors in nevus-cell nevus and malignant melanoma. Melanoma Res 7: 299-305, 1997

8) Suzuki T, Ueda M, Naruse K, Nagano T, Harada S, Imaizumi K, Watanabe S, Ichihashi M. Incidence of actinic keratosis of Japanese in Kasai city, Hyogo, J. Dermatol. Sci. 16(1):74-78, 1997

9) Nagano T, Ichihashi M, et al. Skin cancer screening in Okinawa Japan. J Dermatol Sci 19:161-165, 1999

10) Ichihashi M, et al. Chronic and intensive solar ultraviolet exposure in tropical areas promotes photoaging and skin cancer. Jpn J Tropical Med Hygiene 27:39-41, 1999

11) Araki K, Yamaguchi N, Ichihashi M, et al. Incidence of skin cancers and precancerous lesions in Japanese, risk factors and prevention. J Epidemiol (in press).

12) Takahashi K, Yamaguchi N, et al. Regional correlation between estimated UVB levels and skin cancer mortality in Japan. J Epidemiol (in press)

13) Akiba S, Yamaguchi N, Ichihashi M, et al. Influence of chronic UV exposure and lifestyle on facial skin photo-aging, results from a pilot study. J Epidemiol (in press)