Topical application of Photofrin® for oral neoplasms in animal

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Received 31 January 2005; accepted 15 September 2005

Abstract. Early diagnosis improves oral cancer prognosis. Exact demarcation of tumor margins improves surgical outcomes. This study evaluates Photofrin® fluorescence: a new diagnostic procedure for detection of oral neoplasms in animal models. Fourteen male Golden Syrian hamsters were used. 0.5% D.M.B.A (9,10 dimethyl-1,2-benzanethracene) was brushed onto cheek pouches bilaterally daily for 2 weeks. Hamsters with oral neoplasms received 2.5 mg/ml Photofrin® solution topically. After 3 h the neoplasms underwent fluorescence illumination (λex = 380–420 nm). A quantitative analysis of the fluorescence contrast between the neoplastic and surrounding tissue was performed using the RGB Mode and the Gray Scale. (GS) Statistical analysis was performed using the ANOVA test. Analysis of the 14 hamsters’ 28 biopsies revealed 4 (14.3%) displayed squamous hyperplasia (1 mild, 3 severe) and 24 (85.7%) displayed squamous cell carcinoma. The sensitivity of neoplasms evaluated using the RGB and GS modes combined resulted in 92.15% (in vivo macroscopic image) and 93.45% (histological). The specificity of neoplasms evaluated via RGB and GS modes combined resulted in 94.78% (in vivo macroscopic image) and 97.30% (histological). The difference between healthy tissue and the lesions as a group is statistically significant. Photofrin® fluorescence provides a sensitive, non-invasive technique for early identification of malignant neoplasms in the oral cavities of animal models.

Key words: hamster, photodynamic diagnosis, Photofrin®, oral neoplasms

1. Introduction

If oral cancer is detected and treated early, the surgical success rate is better than that of most other types of cancer. In Taiwan, one of the primary causes of death is malignant tumors. Almost one third (27.08%) of all deaths are caused in this way. Of these malignancies, oral cancer ranks seventh, causing 4.7% of annual deaths, and occurring mostly in the middle-age groups (mean 58 years). The inability to detect oral cancer early results in 10,000 deaths annually. Less than 50% of these patients survive for more than 5 years.

Leukoplekia is the most frequently occurring pre-cancerous lesion of the oral cavity, with a prevalence of 1–4% in the general population. Malignant
transformation occurs in approximately 6% of lesions over 5 years, depending on the lesion type. Traditional treatment options have included regular surveillance and surgical excision, as well as a number of experimental therapies. The standard treatment for early stage (American Joint Committee on Cancer Stage I and II) primary mucosal malignancies of the upper aerodigestive tract (UADT) is surgery and/or radiotherapy. These treatments are frequently ineffective (Hong and Bromer 1983), especially when the tumor is a second primary one. Owing to the field carcinogenic effects of tobacco and betel nut damage, second primary UADT tumors occur in up to 37% of patients (Hong and Doos 1985). In Taiwan, this problem is the principal cause of death in these early stage head and neck cancer patients.

Techniques for early detection are inadequate, and treatment has a high rate of failure in controlling the disease. Further, surgery often results in a high degree of cosmetic and functional or even psychological disability. An alternative to conventional treatment methods involves the use of chemical agents (photosensitizers), which selectively localize in regions of pathology, rendering these tissues fluorescent and/or liable to tissue destruction when exposed to specific wavelengths of light. Photodynamic therapy (PDT) has two specific potential advantages over standard therapy for the treatment of early head and neck malignancies. The first advantage lies with the potential for non-invasive diagnosis – photodynamic diagnosis (PDD). The second advantage is that the lesions can be more effectively monitored, without the need for multiple biopsies to demonstrate the extent or progression of the disease. An additional advantage is the ability of these agents to treat lesions effectively without the field sequelae of ionizing radiation or the cosmetic and functional disabilities associated with surgery. Continued improvement in treatment results for patients with hyperplastic and malignant oral tissue will depend on the ability to cause selective destruction to only the targeted cells, without the production of heat by a non-thermal mechanism. PDT produces a photochemical effect, as opposed to a photothermal effect, which means there is an absence of heat production. This has significant implications as it removes many of the risks associated with the photothermal effect, such as hypertrophic scarring, changes in pigmentation, atrophy and induration. This makes PDT a potentially safer and more effective approach than conventional surgery. Photofrin® has already been approved for clinical application by the FDA in the United States, and can be effectively used for early detection and pre-operative diagnosis, in conjunction with PDT for the treatment of malignancies. This study, however, aims to evaluate PDT using topically applied Photofrin® with protoporphyrin IX (PpIX)-induced fluorescence, as a new diagnostic procedure for the detection of neoplasms in animal oral tissue. These parameters are therefore evaluated in an animal model.