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THE USE OF VELSCOPE® FOR DETECTION OF ORAL POTENTIALLY MALIGNANT DISORDERS AND CANCERS – A PILOT STUDY

WYKORZYSTANIE SYSTEMU VELSCOPE® DO WYKRYWANIA ZMIAN POTENCJALNIE ZŁOŚLIWYCH I RAKÓW W OBRĘBIE BŁONY ŚLUZOWEJ JAMY USTNEJ – BADANIE PILOTAŻOWE

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Summary

Introduction. Cancer is one of the major threats to public health in the world. Oral cancer presents especially low survival rate. Early detection of oral cancer and identification of oral potentially malignant disorders (OPMD) is crucial for improving the outcome of this disease. Adjunctive techniques that may facilitate the early detection of OPMD and oral cancer have emerged in the past decades.

The objective of the present study was to assess the utility of the autofluorescence examination.

Materials and methods. 50 patients, 32 males and 18 females, with oral cavity and lip cancer history were enrolled. Investigation of oral mucosa condition involved the conventional examination in white light and the autofluorescence examination. All detected oral lesions that had not responded to the conservative therapy in 14 days were biopsied.

Results. Oral lesions were detected in 10 patients. Fluorescence visualization loss was observed in eleven of twelve clinically diagnosed lesions. Single lesions were detected only in the conventional or autofluorescence examination. 11 lesions were biopsied. The histopathological examination confirmed dysplasia in 3 cases. 2 lesions were biopsied for the second time. The examination revealed carcinoma in situ and invasive carcinoma. The sensitivity and specificity of autofluorescence for the detection of a dysplastic and cancer lesion was 100% and 12.5%, respectively.

Conclusion. While VELscope® was useful in confirming the presence of oral lesions, the device was unable to discriminate high – risk from low – risk lesions.

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Streszczenie

Wstęp. Rak jest jednym z głównych zagrożeń zdrowotnych na świecie. Rak jamy ustnej charakteryzuje się szczególnie niskim wskaźnikiem przeżywalności. Wczesne wykrycie raka oraz identyfikacja zmian potencjalnie złośliwych w obrębie błony śluzowej jamy ustnej są szczególnie istotne dla poprawy tego wskaźnika. W ostatnich dziesięcioleciach pojawiły się techniki wspomagające, które mogą ułatwić wczesne wykrycie zmian potencjalnie złośliwych i raków w obrębie jamy ustnej.

Celem prezentowanego badania była ocena przydatności badania wykorzystującego zjawisko autofluorescencji.

Materiał i metody. 50 pacjentów, 32 mężczyzn i 18 kobiet, leczonych w przeszłości z powodu raka jamy ustnej lub warg, zostało włączonych do badania. Podczas kontroli onkologicznej stan błony śluzowej jamy ustnej oceniano tradycyjnie wzrokiem w świetle białym oraz

w świetle fluorescencyjnym. Ze wszystkich wykrytych zmian, które nie odpowiedziały na leczenie zachowawcze w ciągu 14 dni, pobrano wycinki.

W y n i k i. Zmiany wykryto u 10 pacjentów. Utratę autofluorescencji zaobserwowano w 11 z 12 zmian, które były widoczne w konwencjonalnym badaniu. Pojedyncze zmiany były widoczne tylko w świetle białym lub fluorescencyjnym. Wycinki pobrano z 11 zmian. Badanie histopatologiczne w 3 przypadkach potwierdziło dysplazję. Z 2 zmian pobrano powtórne wycinki. Badanie histopatologiczne wykazało raka in situ i raka inwazyjnego. Czułość i swoistość autofluorescencji w wykrywaniu zmian dysplastycznych i raków oceniono odpowiednio na 100% i 12,5%.

W n i o s k i. Podczas gdy VELscope® okazał się przydatny do potwierdzania obecności zmian patologicznych, nie wykazano jego przydatności do odróżniania zmian wysokiego ryzyka od zmian niskiego ryzyka transformacji nowotworowej.

Key words: oral cancer, oral potentially malignant disorders, autofluorescence, screening
Słowa kluczowe: rak jamy ustnej, zmiany potencjalnie złośliwe, autofluorescencja, skrining

INTRODUCTION

Oral cancer, traditionally defined as squamous cell carcinoma of the lip, oral cavity and oropharynx, is an increasing problem in many countries [1]. Every year more than 400 000 cases of oral cancer worldwide are diagnosed [2]. In 2009 in Poland, 2477 cases were reported [3].

Despite the development of treatment modalities, the five – year survival rate in oral cancer has remained approximately 50% for the last 50 years [2, 4]. In 2009 in Poland, 1375 cases of death caused by oral cancer were reported [3]. An important reason of poor survival rate in oral cancer patients is usually advanced stage of the disease at the time of diagnosis. Delay in the diagnosis is especially attributed to incomplete awareness of the patient, that even small and asymptomatic oral lesions might have malignant potential, also poor ability of oral health care professionals to detect the early stages of oral potentially malignant disorders (OPMD) and cancerous lesions is relevant [2]. The dental practitioners should not only be aware of the fact that OPMD and other mucosal disorders might have similar clinical presentations [1], but should also know that oral lesions with epithelial dysplasia more often develop into cancer [9, 10, 11, 12].

In patients who were treated for oral cancer, local recurrence of the disease and/or loco-regional metastases are very frequent, especially in the first three years following the surgery [13, 14].

Oral cancer is also associated with the development of multiple primary tumors (MPT). The rate of the second primary tumors/malignancies (SPT/SPM) in these patients is estimated at 1.5 – 8.5% per year [5, 6]. If the first tumor develops in oral cavity or oropharynx, the second primary tumor usually has the same location [7, 8].

To improve poor results of the treatment, the public awareness of the importance of regular oral screening should be increased and new diagnostic aids that could help general dentists identify high-risk oral lesions, should be used.

Autofluorescence examination is one of potential techniques that may be used to improve the visualization and assessment of OPMD and oral cancer [1]. It is used in VELscope® - a non-invasive, direct tissue fluorescence visualization system.

This device emits a particular wavelength (400 – 460 nm) and intensity of light that illuminates the oral mucosa and excites natural fluorophores in the tissues. The tissues emit fluorescence that is visualized through the special filters [15]. Normal oral mucosa emits a pale green autofluorescence, whereas abnormal or suspicious lesions exhibit loss of autofluorescence and appear dark by comparison to the healthy tissue [2].

The aim of the study was to evaluate oral mucosa condition in patients who underwent treatment for oral cavity or lip cancer with the use of an autofluorescence imaging system (VELscope®) and its utility to detect and evaluate oral potentially malignant disorders and cancer lesions.

MATERIALS AND METHODS

Fifty patients (32 males and 18 females) with oral cavity or lip cancer history treated in the Department of Maxillofacial Surgery at Rydygier's Hospital in Cracow were enrolled in the study. Investigation of oral mucosa condition involved conventional clinical visual examination and autofluorescence examination. All detected oral lesions (only in conventional or autofluorescence examination and in both), that had not responded to the conservative therapy after 14 days, were biopsied. The study was approved by Bioethical Committee of the Jagiellonian University.

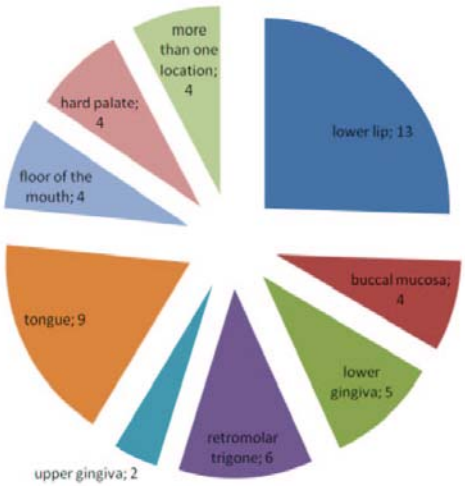

Fig. 1. *The location of the first tumor in examined patients*
Ryc. 1. *Lokalizacja pierwszego guza w badanej grupie pacjentów*

Following the clinical examination under an incandescent light source, clinical diagnosis was established. Autofluorescence examination was performed using VELscope® (Visually Enhance Lesion Scope) under dimmed room light, with the protective eye wear worn by the patient throughout the procedure. The areas of fluorescence visualization loss (FVL) identified by the VELscope® were taken into consideration. In some cases, further diagnostic methods (such as microbiological assessment) were introduced. The lesions were being treated due to the clinical and microbiological diagnosis for 14 days. If there had been no improvement, a surgical biopsy was performed for histopathological assessment of lesions.

The results of clinical and autofluorescence examination of oral mucosa were compared. Using histology as a gold standard, sensitivity and specificity of the autofluorescence test for distinguishing dysplasias and cancers (high-risk oral lesions) from other oral lesions (benign oral lesions) were calculated.

RESULTS

Thirteen pathological lesions were detected in ten patients (20%). Nine patients had single lesion, whereas one had multiple ones. FVL was observed in eleven of twelve (91.7%) clinically diagnosed pathological lesions. In autofluorescence examination, there was one area of FVL detected, that was not visible in incandescent light source. Two lesions were totally cured after 14-days conservative therapy. Eleven lesions were biopsied. Oral epithelial dysplasia was confirmed in three lesions (27.3%). Due to complete loss of fluorescence within two lesions, they were biopsied again, using VELscope® to choose the precise biopsy side. The histopathological assessment confirmed carcinoma in situ and invasive carcinoma. These lesions were diagnosed as SPM and the rate of SPM was estimated at 4%. Autofluorescence examination showed a sensitivity of 100%, as all high – risk oral lesions showed FVL. However the autofluorescence was not highly specific for dysplasias and cancers, as FVL was observed in 7 (87.5%) of the benign oral lesions, leading to a low specificity of 12.5%.

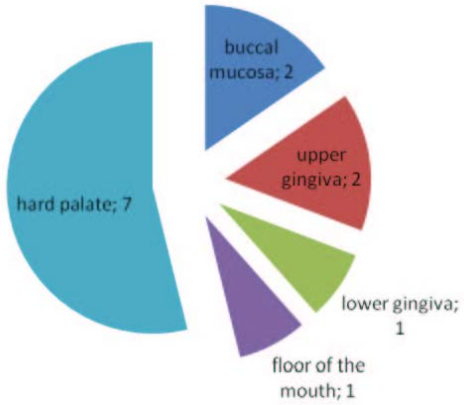

Fig. 2. *The location of detected oral lesions in examined patients*
Ryc. 2. *Lokalizacja wykrytych zmian w badanej grupie pacjentów*

Table. I. *The comparison of histopathological, clinical and fluorescence examination's results*
Tabela. I. *Porównanie wyników badania histopatologicznego, klinicznego i fluorescencyjnego*

Clinical examination	Fluorescence examination	Histopathological examination				
		dysplasia (-)	**dysplasia (+)**	**cancer**	Subtotal	Total
white stain	**FVL**	2	0	0	**2**	**3**
	green fluorescence	1	0	0	1	
red stain	**FVL**	1	0	0	**1**	**1**
	green fluorescence	0	0	0	0	
white/red stain	**FVL**	1	2	1	**4**	**4**
	green fluorescence	0	0	0	0	
ulceration	**FVL**	1	1	1	**3**	**3**
	green fluorescence	0	0	0	0	
hyperplastic lesion	**FVL**	1	0	0	**1**	**1**
	green fluorescence	0	0	0	0	
unchanged mucosa	**FVL**	1	0	0	**1**	**1**
	green fluorescence	0	0	0	0	
Total		**8**	**3**	**2**	13	13

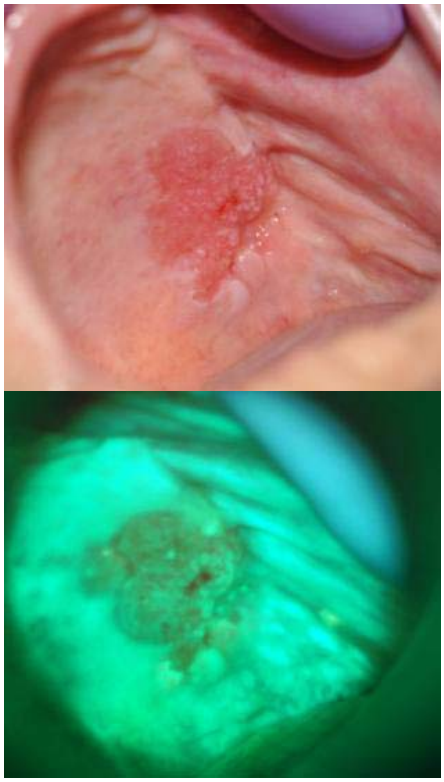

Fig. 3. *78 – year – old patient with the hard palate cancer*
Ryc. 3. *Pacjent lat 78, rak podniebienia twardego*

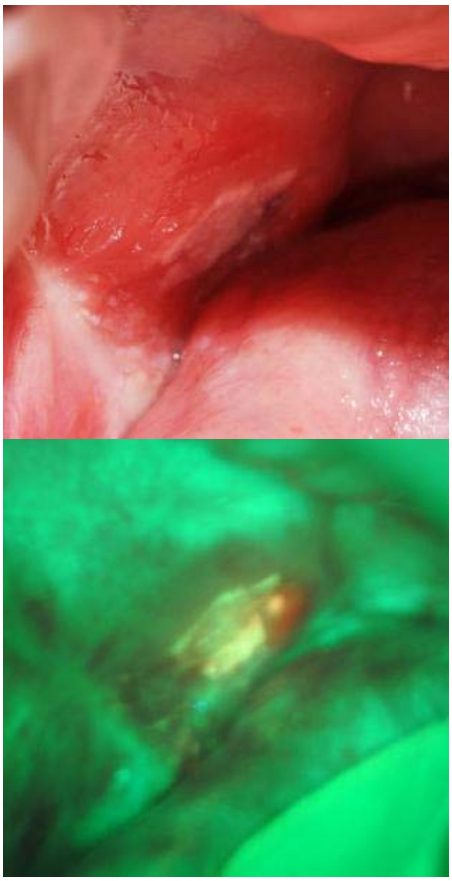

Fig. 4. *62 – year – old patient with the buccal mucosa cancer*
Ryc. 4. *Pacjent lat 62, rak błony śluzowej policzka*

DISCUSSION

The condition of oral mucosa should be thoroughly examined during every visit in dental practice, especially in patients with oral cancer risk factors. In our study pathological lesions were diagnosed in 20% of patients with oral cavity and lip cancer history at the time of their oncological follow-up. However, not all dentists have wide experience in OPMD and oral cancer detection that leads to the failure in early detection of these lesions. There are many adjunctive techniques for oral cancer examination and lesions diagnosis. The utility of autofluorescence as a diagnostic test, especially its accuracy in the detection of oral epithelial dysplasia and cancer, was assessed in this study.

FVL was observed in all cases (100%) that were histopathologically diagnosed as dysplasia and cancer. This outcome demonstrates the ability of the technique to detect high – risk lesions. However, it was disappointing to note that autofluorescence examination gave positive result also in majority of other lesions (without dysplasia). This finding re-affirms the lack of specificity of the technique for the detection of dysplasia and cancer by this device.

Comparison of the results of this study with other published data is not easy, due to limited studies in literature reporting sensitivity and specificity of the device. Lane et al. investigated the ability of VELscope® to identify precancerous or cancer lesions [16]. The study consisted of 44 patients who had history of oral dysplasia or HNSCC (head and neck squamous cell carcinoma). After conventional oral examination, the oral cavity was evaluated with VELscope® to identify areas of FVL. Using histology as the gold standard, the device demonstrated 98% sensitivity and 100% specificity when discriminating normal mucosa from severe dysplasia/carcinoma in situ (CIS) or invasive carcinoma. Data presented in this study demonstrated significantly lower specificity (12.5%) for the technique. It is supposedly due to several benign disorders detected, thus reducing the 'spectrum bias' encountered in published studies – a desirable feature of this study. Awan et al. evaluated the accuracy of autofluorescence against conventional oral examination and surgical biopsy [1]. The study consisted of 126 patients with oral white and red patches, suspicious of OPMD. Following conventional visual and autofluorescence examination, all lesions were biopsied and histopathologically assessed. The

sensitivity and specificity of autofluorescence for the detection of a dysplastic lesion was 84.1% and 15.3% respectively. These results are similar to the ones obtained in our study.

Huber at al. [17] and Huff et al. [18] reported contrasting results on the utility of VELscope®. The Huber's study did not prove that the autofluorescence examination detects any additional suspicious lesions not identified by conventional oral examination. Moreover, VELscope® interpretation did not enhance the clinical management of the suspicious lesions. Several commonly occurring conditions, such as mucosal pigmentations, ulcerations, irritations, and gingivitis were associated with a loss of fluorescence using VELscope®. On the other hand, Huff et al. reported an increase in prevalence of mucosal disorders with epithelial dysplasia in a cohort of patients subjected with VELscope®, compared to the same cohort examined with incandescent light only. In the present study, only one additional lesion was identified in the autofluorescence examination in comparison with the conventional examination; however , the histopathological assessment of this lesion did not confirm dysplasia. To acknowledge the VELscope® system's added value to conventional visual examination, further studies are necessary.

CONCLUSIONS

Oral mucosa in patients with oral cavity or lip cancer history should be thoroughly screened in the follow-up examination, due to the risk of recurrence of the tumor or development of a new primary malignance and oral potentially malignant disorders. High sensitivity of the autofluorescence examination might be helpful in detection of high-risk oral lesions and could be recommended for oral cancer screening. However, due to the low specificity of the autofluorescence examination for discriminating dysplasias and cancers from benign oral lesions, VELscope® could not be recommended as the decisive diagnostic tool and final diagnosis should be based on histological examination.

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