PD AND PDT OF PRECANCEROUS DISEASES OF THE ORAL CAVITY AND LARYNX AFTER SUBLINGUAL ADMINISTRATION OF 5-ALA

P.M. Alekseeva¹², K.T. Efendiev¹², A.A. Shiryaev³, M.A. Rusakov³, S.I. Samoilova³, I.V. Reshetov³, V.B. Loschenov¹²

¹ Prokhorov General Physics Institute of the Russian Academy of Sciences, Moscow, Russia
² National Research Nuclear University MEPhI (Moscow Engineering Physics Institute), Moscow, Russia
³ Sechenov First Moscow State Medical University, University Clinical Hospital No.1, Levshin Institute of Cluster Oncology, Moscow, Russia

E-mail: alekseeva.polina2012@mail.ru

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The relevant problems of modern oncology are timely diagnosis and effective treatment of precancerous conditions of the oral cavity and larynx. The lack of timely diagnostics and treatment of precancerous conditions contributes to their further transformation into a malignant tumor.

562,328 new cases of oral and laryngeal cancer were identified in 2020 [1].

The 5-year relative survival rate is about 50% [2].

The study aimed to develop a method for sublingual administration of 5-ALA to patients and to evaluate its effectiveness in fluorescent diagnosis and photodynamic therapy of neoplasms of the oral cavity and larynx.

Fig. 1. The incidence of cancer of the oral cavity and larynx among men and women of all ages in the world in 2020


Clinical characteristics

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Investigated zones</th>
<th>Power density, W/cm²</th>
<th>Energy density, J/cm²</th>
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<td>Dysplasia of the oral cavity</td>
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</table>
Materials

Before PD and PDT, a sublingual solution with 5-ALA was administrated into the sublingual cavity in small portions.

- The volume of the entire solution for one patient is 7-10 ml.
- The total keeping time of the entire volume of the solution is 10-15 minutes.

Solution are quickly absorbed into the oral mucosa through the blood vessels under the tongue, bypassing the extremely unfavorable environment in the gastrointestinal tract.

5-ALA induces protoporphyrin IX (PpIX) in biotissue cells, which is a fluorescent precursor on the heme biosynthesis pathway.

- The accumulation time of PpIX in the cells of pathological biological tissue is 2 hours.

Fig. 2. Sublingual solution composition (pH = 5-6)

| 5-ALA 20 mg/kg (pH=2-3) | NaHCO₃ (1:10) | C₁₂H₂₂O₁₁ |
Methods and equipment

Fig. 4. The scheme of the study of pathological tissue

Fig. 5. Photodynamic therapy

Fig. 6. The investigated zones of the oral cavity
Results of video-fluorescence diagnostics of a patient with oral dysplasia

Fig. 7. Images of the oral mucosa of a patient with **mild dysplasia** before and after PDT ($E = 100 \text{ Дж/см}^2$); **a.** Fluorescent mode; **b.** Color mode; **c.** Combined mode (the fluorescence index is displayed in the corners of the image).
Results of spectral fluorescence diagnostics of patients with laryngeal papillomatosis and oral leukoplakia

Fig. 8. Results of spectral fluorescence diagnostics of patient with larynx papillomatosis. **a.** Fluorescence spectra of the normal and pathological larynx mucosa before and after PDT ($E = 200 \text{ Дж/см}^2$); **b.** Fluorescence indices.

Fig. 9. Results of spectral fluorescence diagnostics of patient with oral leukoplakia. **a.** Fluorescence spectra of the normal and pathological oral mucosa before and after PDT ($E = 200 \text{ Дж/см}^2$); **b.** Fluorescence indices.
Endoscopic images of the larynx mucosa of a patient with larynx papillomatosis

Fig. 10. Endoscopic images of the larynx mucosa of a patient with larynx papillomatosis. 
  a. Before PDT; b. 6 days after PDT.
Results of histological investigation of biological material from patient with mild oral dysplasia

Fig. 11. Results of histological investigation. 

a. Before PDT; fragment of the mucous membrane of patient with mild dysplasia (mild flat epithelial neoplasia); 

b. After PDT; acanthosis, necrosis of the superficial layers of the stratified squamous epithelium; 

c. After PDT; epithelial layer with preserved stratification, necrosis of the superficial layers of the stratified squamous epithelium; 

d. After PDT; angiomatosis of the subepithelial base with fibrin thrombi in the lumen of the capillaries. Hematoxylin-eosin staining.
The effectiveness of sublingual administration of 5-ALA for PD and PDT in precancerous diseases of the oral cavity and larynx has been demonstrated.

Sublingual administration of 5-ALA has several advantages compared to other methods of administration:

1. Glucose supports the active transport of 5-ALA into cells.
2. Medical and diagnostic procedures in patients can be carried out independently of the tumor location.
3. The possibility of aspiration during the anesthesia administration is avoided.

However, the sublingual administration of 5-ALA to patients with diabetes mellitus requires caution since the solution contains glucose.
Thank you for the attention!