Conference Paper

Clinical Experience of Luminescent Diagnostics of Precancerous Diseases and Cervical Cancer

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Abstract

The article summarizes the experience of using luminescent diagnostics with the use of ytterbium porphyrin complexes in gynecology and oncology. A pharmaceutical composition based on the Yb complex of 2,4-dimethoxyhematoporphyrin IX was used as the luminescent markers within the infrared range. The determination of luminescence characteristics (luminescence intensity) was carried out using a laser-fiber fluorimeter in the range of 900-1100 nm. A new method for diagnosis of cervical disease has been proposed. The method of luminescent diagnostics allows to conduct a survey of a large number of patients in a short time. The method of luminescent diagnostics using the ytterbium complexes of porphyrins is not invasive. The method can be used as a screening. Differences between normal and pathologically altered cervical tissue have been identified and differences between pathological changes in the cervix HSIL (CIN II, CIN III) and cervical cancer are reliable.

Keywords: Cervical cancer, squamous cell carcinoma, diagnosis of cervical cancer, squamous intraepithelial lesions of high grade – HSIL, luminescent diagnostics, luminescing in the near infrared (NIR) spectral region, porphyrins, ytterbium complexes of porphyrins.

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1. Introduction

Relevance. In Russia, for 10 years from 2005 to 2014, the incidence of cervical and uterine cancer increased by 49.2% (from 39.4 to 58.8 cases per 100,000 women) [1]. There is a directly proportional relationship between the stage at which the diagnosis

is made and the effectiveness of therapy, long-term results, and after-treatment life expectancy. The earlier the diagnosis is made, the better are results of treatment. The optimal option is timely, early detection of precancerous processes.

These data indicate the high urgency of the problem of early diagnosis of cervical cancer. An accessible method that would allow for examining large patient arrays groups for early diagnosis of precancerous cervical conditions has not yet been put into practice. The use of ytterbium complexes of porphyrins (YCP) luminescing in the near infrared (NIR) spectral region of 900 nm - 1100 nm opens up great prospects in this direction [2–4].

2. Purpose of the study

To develop a method for detecting precancerous diseases and cervical cancer on the basis of laser luminescence diagnostics with the help of ytterbium porphyrin complexes.

3. Materials and methods

Under control, there were 90 women divided into three groups. The first group included healthy women without pathology of the cervix. The second group included women with squamous intraepithelial lesions of high grade (HSIL) in the Bethesda classification (The Bethesda System (TBS) 1988, 1991). The third group included women with cervical cancer.

Women measured the luminescence level of the cervix tissue after they were sensitized with YCP. The Fliroscan gel was used as an YCP carrier. The gel is officially registered in Russia and the countries of the customs union. The registration number of the declaration on the conformity of the vehicle No.RU D-RU.AI018.B.06317 dated 09.02.2016. A pharmaceutical gel composition based on the Yb complex of 2,4-dimethoxyhematoporphyrin IX was used as a luminescent marker.

Figure 1 shows the absorption spectrum of the ytterbium complex of the dipotassium salt of 2,4-dimethoxyhematoporphyrin IX.

The luminescence characteristics were studied with a laser-fiber fluorimeter in the range of 900-1100 nm. The measuring complex includes a semiconductor laser (λ = 405 nm, P = 30 mW), a block of interference filters, a multi-core high-aperture fiber-optic probe, a photodiode array with a preamplifier. Laser-fiber fluorimeter operates in the spectral range of 900-1100 nm. The IR area of the spectrum (760-1300 nm) is

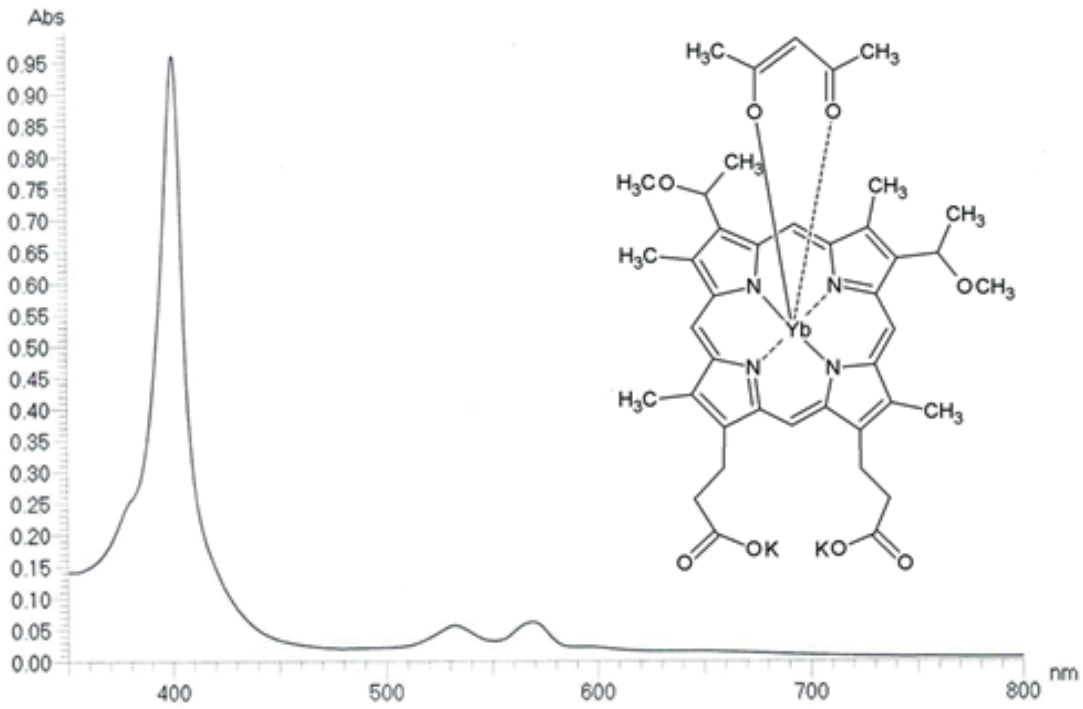

Figure 1: The electronic absorption spectrum of the ytterbium complex of the dipotassium salt 2,4-dimethoxyhematoporphyrin IX (40% solution, concentration of the complex - 10^{-5} M).

considered to be the "transparency window" for biological tissues and is characterized by minimal absorption and practically no background luminescence of endogenous chromophores in this spectral area.

Laser-fiber fluorimeter allows simultaneous irradiation of the cervical tissues with laser radiation in the range of the Sore strips and measuring the integrated intensity of the luminescence in the IR area of the spectrum.

4. Results

Reliable ($P < 0.001$) differences between 1, 2 and 3 groups in terms of luminescence level were revealed. The intensity of luminescence from the cervical tissues without pathological changes ranged from 0.016 to 0.026 mV (Figure 2).

The intensity of luminescence from cervical tissue with squamous intraepithelial lesions of high degree (HSIL) increased to 0.25-0.75 mV (Fig. 3, 4).

The intensity of luminescence from tissues in cervical cancer increased to 5.5-6.0 mV (Figure 5).

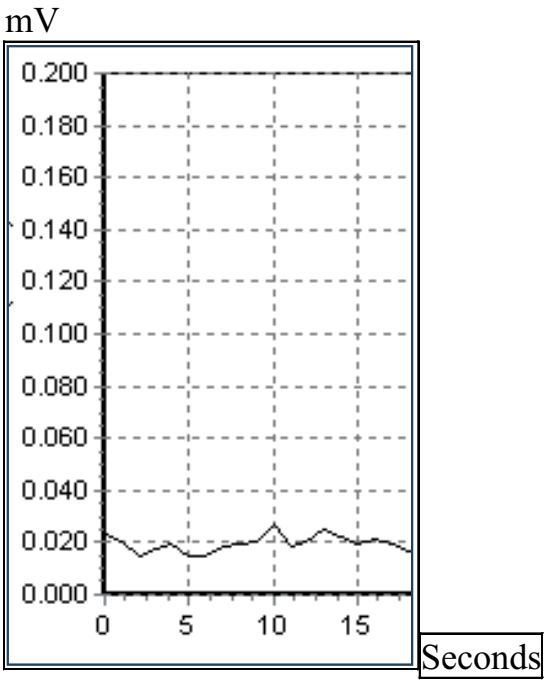

Figure 2: Intensity of luminescence from cervical tissues without pathological changes.

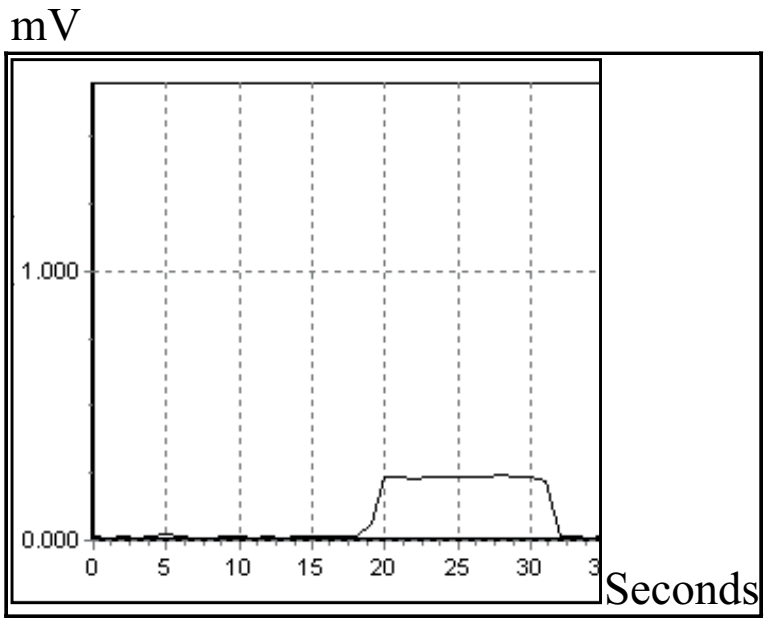

Figure 3: Intensity of luminescence from cervical tissue with HSIL (CIN II).

5. Conclusions

1. The method of luminescent diagnostics makes it possible to reveal objective differences between morphologically normal and pathologically altered cervical tissues.

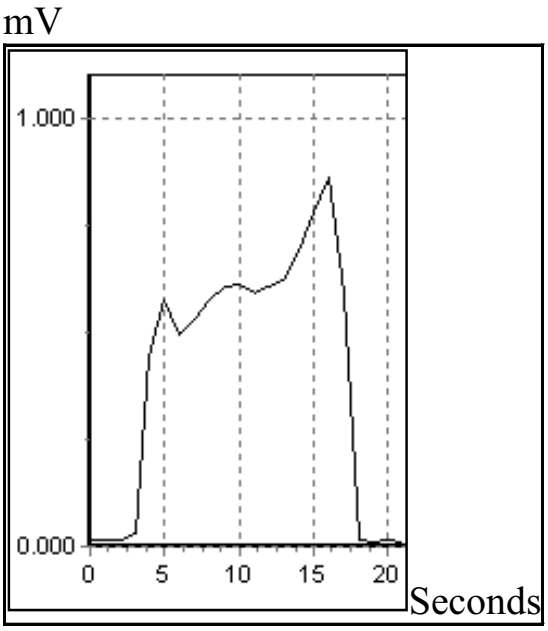

Figure 4: Intensity of luminescence from cervical tissue with HSIL (CIN III).

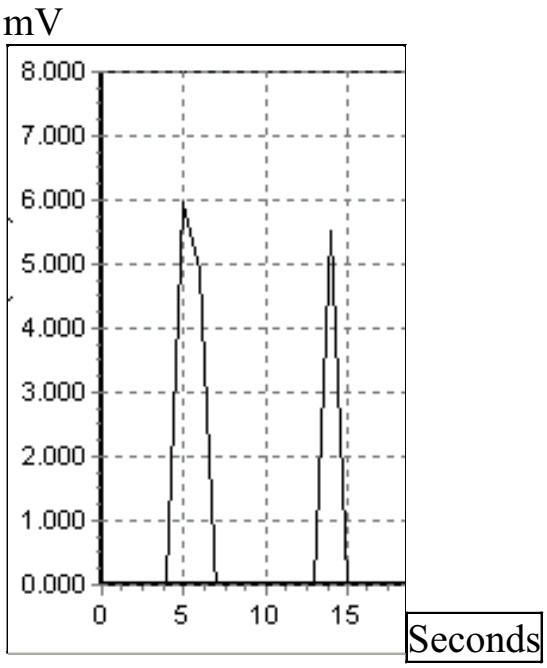

Figure 5: The intensity of luminescence from tissues in cervical cancer.

2. The method is highly sensitive - the intensity of luminescence of the cervical tissues with HSIL (CIN II) increases by 10 - 16 times.
3. With HSIL (CIN III), the luminescence intensity of the CMM tissues increases by 26 to 47 times.
4. With cancer, the intensity of luminescence from the cervical tissue with increases by 200 to 300 times.

5. The difference in luminescence intensity between normal and pathologically altered tissues is significant (P <0.001).

6. The study of the level of luminescence is a promising direction for the development of a new method for detecting pathological conditions in gynecology.

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