COMPARISON OF 5-AMINOLEVULINIC ACID BASED FLUORESCENCE DIAGNOSTICS WITH HISTOLOGY IN THE DETECTION OF CERVICAL NEOPLASIA

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Introduction

Cervical cancer is the second most common type of cancer in females.

500 000 women in the world are diagnosed each year with invasive cervical cancer.
Healthy woman

HPV

Low grade cervical intraepithelial neoplasia – CIN 1

CIN 2

CIN 3 (carcinoma in situ)

Invasive cancer

Present-day diagnostic methods - screening program

Pap test (cytology)

- Poor sensitivity (false negative rate of 30-87%).

- Poor specificity (average 52%).

Nowadays one of the most promising photosensitizers is becoming Protoporphyrin IX (PpIX).

To induce PpIX accumulation in target tissues often is used 5-aminolevulinic acid (5-ALA).

The aim of the study

To investigate the diagnostic potential of 5-aminolevulinic acid induced Protoporphyrin IX fluorescence in patients with cervical intraepithelial neoplasia and compare it with histology.
Methods. (1)

Patient with suspected CIN according to abnormal cervical cytology.

18 nonpregnant women with a mean age of 36 years (range 23-57 years).

**Colposcopy**

Application of 3g 3% ALA creame on cervical surface

Repeted recording of fluorescence spectra after 100-180 minutes
Methods. (2)

Fig. 1. Scheme of the fluorescence spectroscopy system used for fluorescence fotodetection of cervical lesions.

Fig. 2. Colposcopic view of the cervix and conventional marking of the quadrants.
Fig. 4. Fluorescence spectra from neoplastic and normal cervical tissue before ALA application (A) and after (B).
Analysis of measured fluorescence spectra

\[ R = \frac{I(634 \text{ nm})}{I(510 \text{ nm})} \]

Fig. 3. Typical fluorescence spectra from neoplastic cervical tissue with autofluorescence (510 nm) and Protoporphyrin IX (634 nm) maximums.
Results. (2)

Fig. 5. $R = \frac{I(634)}{I(510)}$ ratio values depending of cervical tissue state.
Table 1. Ratios of fluorescence intensities for different diagnosis.

<table>
<thead>
<tr>
<th>Patient</th>
<th>$R_{\text{healthy}}$</th>
<th>$R_{\text{CIN3}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>3.2</td>
<td>17.9</td>
</tr>
<tr>
<td>2.</td>
<td>4.7</td>
<td>39.2</td>
</tr>
<tr>
<td>3.</td>
<td>5.3</td>
<td>100.1</td>
</tr>
<tr>
<td>4.</td>
<td>0.7</td>
<td>8.2</td>
</tr>
<tr>
<td>5.</td>
<td>9.7</td>
<td>80.1</td>
</tr>
<tr>
<td>6.</td>
<td>7.1</td>
<td>25.7</td>
</tr>
<tr>
<td>7.</td>
<td>1.3</td>
<td>6.5</td>
</tr>
<tr>
<td>8.</td>
<td>6.4</td>
<td>98.3</td>
</tr>
<tr>
<td>9.</td>
<td>6.5</td>
<td>30.3</td>
</tr>
<tr>
<td>10</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>2.8</td>
<td>35.8</td>
</tr>
<tr>
<td>13</td>
<td>0.9</td>
<td>5.4</td>
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<tr>
<td>14</td>
<td>0.33</td>
<td>9.9</td>
</tr>
<tr>
<td>15</td>
<td>7.9</td>
<td>41.5</td>
</tr>
<tr>
<td>16</td>
<td>8.4</td>
<td>137</td>
</tr>
<tr>
<td>17</td>
<td>3.2</td>
<td>54</td>
</tr>
<tr>
<td>18</td>
<td>0.4</td>
<td>17.9</td>
</tr>
<tr>
<td>Average</td>
<td>$4.4 \pm 3.1$</td>
<td>$44.2 \pm 39.6$</td>
</tr>
</tbody>
</table>

$R_{\text{healthy}}$ – is the ratio of the measured place from histologically confirmed non neoplastic tissue;

$R_{\text{CIN3}}$ – is the highest ratio of quadrant, in which CIN3 was proved histologically;

$$\frac{R(\text{healthy})}{R(\text{CIN3})} = 8.6$$
Results. (4)

CIN 3
R=2.2
No neoplasia

CIN 1
R=4.9
No neoplasia

CIN 1/2
R=9.2
CIN 3

No neoplasia

CIN 1/2
R=19.2

No neoplasia

No neoplasia
Conclusions

- 5-ALA induce PpIX accumulation in cervical tissues.
- The diagnostics of each quadrant according fluorescence spectra should be done on the basis of the highest intensity ratio from each quadrant.
- The $R_{\text{CIN3}}$ should be 8.6 times higher than $R_{\text{healthy}}$.
- Higher ratio corresponds to higher grade neoplasia.
Thank you for your attention.