

MORPHOLOGICAL CRITERIA FOR THE EFFICIENCY OF INTRAVEIN LASER THERAPEUTIC TREATMENT OF DYSPLASTIC PROCESSES IN THE STOMACH MUCOSA

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We present some data on the dynamics and quantitative estimation of the dysplastic processes in the stomach mucosa at the intravein laser therapy. The group of patients observed in this study consisted of 96 persons with the chronic gastric ulcer and chronic atrophically-hyperplastic gastritis. In 74 patients we have revealed epithelium dysplasia of different severity. In this group of patients we have carried out quantitative cytometry that enabled us to reliably distinguish, by the indications studied, among the dysplasia of I, II, and III degrees. We have found from this study that the intravein laser therapy produces a pronounced effect on the stomach mucosa morphology. Thus, in 81.1% cases we have observed a complete regression of the I and II degree dysplasia. In 13.5% patients a regression of the II and III degree dysplasia to the I degree one, and in 6.4% cases with the III degree dysplasia the dysplastic process has been stabilized. The results obtained in this study are a good evidence of the intravein laser therapy efficiency in correcting precancer modifications of the stomach mucosa.

Diagnostics of the gastric cancer at its early stage needs for refining the morphological criteria of precancer modifications of the stomach mucosa.^{5,6} The term dysplasia has been accepted by the WHO Expert panel, in 1978, as an indicator of precancer modifications in the stomach mucosa allowing one to reveal enhanced risks of all precancer diseases of stomach.^{9,10} The dysplastic changes cover the morphological signs as broken cell typing, violation of the cell differentiation, and changed mucosa structure.

However, the dysplasia is still only poorly studied, regardless of vast literature on the precancer gastric diseases and experimental data on the biopsy and operative samples. It is also the matter of fact that no versatile technique exists for making cytological diagnostics of the epithelial dysplasia of the stomach mucosa.^{3,7,8}

When analyzing the material, authors normally estimate the degree of cell proliferation and cell typing violation, following the WHO classification of 1983 and that developed at Oncological Center of the Russian Academy of Sciences (1985), pointing out only heavy dysplasia. At the same time, use of new morphometric methods of quantitative analysis may increase the information content of the dysplasia diagnostics.

Since the probability of carcinoma development on the background of (or from) the dysplastically changed epithelium of the stomach mucosa (SM) the

development of highly efficient methods of correcting the above states is very urgent for the prophylaxis of the gastric cancer.

During two recent decades the low-intensity laser radiation is being more and more widely used in clinical medicine and, in particular, in gastroenterology and oncology. Results of many studies^{1,2,4,11,12} showed the anti-inflammatory and regenerative effect of laser radiation well pronounced in curing the gastric ulcer and atrophic processes in the stomach mucosa. The results we have obtained in our studies¹³ also demonstrate the prospects of using this kind of therapy as a mean for secondary prophylactics of the gastric cancer that is pathogenically justified.

Taking all the above said into account we present in this paper some quantitative estimates of the dysplastic processes effect in the stomach mucosa and consider their dynamics after the intravein laser irradiation of the blood (IVLIB).

TECHNIQUE

The investigation technique used is based on analysis of the bioptic samples and touch smears from the stomach mucosa. The group of patients observed consisted of 96 persons with the histologic diagnosis of chronic gastric ulcer (46 patients) and chronic atrophically hyperplastic gastritis (50 patients). The bioptic samples have been immediately fixed in 12%

formalin. The preparations have been made following a conventional technique and then stained with hemotoxilin and eosin. The touch smears have been stained following Lieshman method with an additional staining with azure-eosin mixture.

The quantitative estimates in the cytological preparations were made using an "Integral 2MTB cytological analyzer of tumor cells. In the analysis made we have determined the area of a cell and its nucleus, the cell perimeter, the area-to-perimeter ratios of the cells, and the shape factors of the cell and its nucleus, as well. Analysis has been made over 100 cells in each cytological preparation. Cytometric data on 22 patients with no dysplastic changes in the epithelium of stomach mucosa were used as a control reference data.

In histological preparations we counted mitotic figures per 1000 cells.

From the whole group of patients observed 74 persons (41 with the chronic gastric ulcer and 33 with the chronic atrophically hyperplastic gastritis) received the intravein laser therapy following the technique we developed earlier. The technique assumes using an LG-75 He-Ne laser that delivers 5 to 6 mW power. The course of this laser therapy lasted 7 days with one 30-min-long seance a day. In all cases the patients were observed with a fibergastroscope before and after the laser treatment accompanied by taking bioptic samples (7 to 10 fragments per a patient).

RESULTS

The cytological and histological analyses of the preparations enabled us to identify the stomach mucosa dysplasia of different degree in 74 patients while in 22

patients no dysplastic changes were revealed. The data obtained in this study are summarized in Table I in accordance with the dysplasia degree and nosological form.

TABLE I. Summary of the clinical data obtained in accordance with the dysplasia degree and nosological forms.

| Degree of dysplasia | Chronic ulcer | Chronic atrophically hyperplastic gastritis | Total |
|---------------------|---------------|---|-------|
| I | 20 | 21 | 41 |
| II | 10 | 11 | 21 |
| III | 11 | 1 | 12 |
| Not revealed | 5 | 17 | 22 |
| Total | 46 | 50 | 96 |

In the case of the Ist degree dysplasia there occurred a weak proliferation of the epithelium, inessential polymorphism, and enlargement of nuclei. In all the cases studied at the IInd degree dysplasia there occurred eosinophilic infiltration while in the case of the IIIrd degree dysplasia the neutrophilic infiltration occurred. In the cases of dysplasia of both the IInd and IIIrd degree we recorded hyperplasia of lymphoid follicles. In 19 patients with the dysplasia of the IInd degree we have revealed intestinal metaplasia. At the morphological diagnosis of dysplasia we have identified a weak or moderate hyperplasia of the cells with atypia. The cytometric results obtained are given in Table II.

TABLE II. Cytometric parameters of the stomach mucosa cells under different-degree dysplasia.

| Groups | Number of patients | Area, μm ² | | Perimeter, μm | The nucleus cytoplasmatic ratio |
|---------------|--------------------|------------------------------|-------------------------------|-------------------------------|---------------------------------|
| | | cell | nucleus | | |
| Control | 22 | 219±23.1 | 98.11±15.3 | 109.27±2.9 | 0.363±0.19 |
| Dysplasia I | 41 | 226±43.4 | 109.1±17.7 | 111.18±2.3 | 0.397±0.24 |
| Dysplasia II | 21 | 487±31.9 <i>p</i> < 0.05 | 163.2±41.2 <i>p</i> < 0.05 | 158.23±3.1 <i>p</i> < 0.05 | 0.613±0.26 <i>p</i> < 0.05 |
| Dysplasia III | 12 | 787±113.3 <i>p</i> < 0.05 | 438.9±27.2 <i>p</i> < 0.05 | 379.27±3.8 <i>p</i> < 0.05 | 0.943±0.06 <i>p</i> < 0.05 |

p is the confidentiality level.

As seen from Table II no reliable differences can be pointed out between the patients from the control group and the group with the Ist degree dysplasia while the patients from the groups with the IInd and IIIrd degree dysplasia differ from the patients in the control group and between the two groups as well. The mitotic index at the Ist degree dysplasia was 2% while in the

case of IInd and IIIrd degree dysplasia it was 5 and 6.9%, respectively.

In patients that have received the intravein laser therapy we repeatedly made the morphometric estimates of the parameters under study, after the treatment course, what allowed us to assess the therapeutic method proposed more objectively.

Analysis made showed a complete regression of the dysplastic process at the Ist and IInd degree dysplasia. In only two patients with the diagnosis of chronic gastric ulcer with the IInd degree dysplasia the regression took place to the Ist degree dysplasia. In eight patients with the IIIrd degree dysplasia of the stomach mucosa epithelium we have recorded the regression to the Ist degree dysplasia and in four patients the dysplastic process has at least stabilized.

Besides, in these same groups of patients we have recorded the following qualitative changes. Thus, the eosinophilic infiltration that took place in the initial state lasted out only in one patient while the neutrophilic one lasted out in all cases. Hyperplasia of lymphoid follicles has been observed already at the Ist degree dysplasia that may be considered to be a result of stimulating effect of the intravein laser therapy on the immune system. The intestinal metaplasia has lasted out in four patients.

In patients with a partial regression of the IInd and IIIrd degree dysplasia the mitotic index was equal to 2.7%. In four patients with the IIIrd degree dysplasia of the stomach mucosa, the case when the process has stabilized, the proliferative activity kept unchanged at the level of 6.2%.

So convincingly positive results of the morphological analysis well agree with the data of endoscopic observations of the patients with gastric ulcer and chronic atrophically hyperplastic gastritis that received the intravein laser therapy. Thus, the data of a control fibergastroscopy showed that in 74.1% of patients there occurred complete skinning over of the ulcer defect and disappearance of the gastritis pattern. In 19.3% of patients we have observed a partial skinning over of the ulcer at a significant weakening of the disease syndrome. Only in 6.6% of cases no any pronounced effect from the treatment given has been observed at fibergastroscopy.

CONCLUSIONS

1. A statistically reliable increase in the cytophotometric parameters of the cells and nuclei is being recorded with increasing degree of the dysplastic process in the stomach mucosa.

2. The intravein laser therapy produces a pronounced effect on the stomach mucosa morphology that results in a full regression of the Ist and IInd dysplasia in 81.1% of cases, partial regression of the IInd and IIIrd dysplasia to the Ist degree one in 13.5% cases, and only in 6.4% cases the dysplastic process of the IIIrd degree stabilized.

3. The morphological criteria proposed may be useful when estimating quantitatively the therapeutic effect of a treatment including, in particular, the intravein laser irradiation of blood.

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