ПРОБЛЕМИ ЗАГАЛЬНОЇ ХІРУРГІЇ

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Шляхи підвищення ефективності хірургічного лікування хворих з новоутвореннями легенів

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Ways of enhancement of the surgical treatment efficacy in treatment of patients, suffering pulmonary tumors

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Реферат

Мета. Визначити ефективність ендоскопічної бронхосанації для профілактики до– та післяопераційних ускладнень у хворих з новоутвореннями легенів.

Матеріали і методи. Вивчено ефективність ендоскопічної фотодинамічної терапії за розробленою авторами методикою з уведенням у трахеобронхіальне дерево водного розчину барвника метиленового синього в концентрації 0,04%, опроміненого лазером з довжиною хвилі 0,63 мкм, самостійної і в поєднанні зі стандартною протизапальною терапією як передопераційної підготовки трахеобронхіального дерева у хворих з раком легенів. У дослідження включено 181 пацієнта з раком легенів II–III стадії, морфологічно підтвердженим, та супутнім ендобронхітом.

Результати. За даними аналізу титру і характеру патогенної мікрофлори в просвіті бронхіального дерева після проведеної передопераційної підготовки встановили, що у разі застосування самостійної ендоскопічної бронхосанації у 55 (87%) спостереженнях патогенної мікрофлори не було. У разі поєднання фотодинамічної бронхосанації зі стандартною терапією патогенну мікрофлору не виявлено у 52 хворих. У разі стандартної підготовки без використання лазерної терапії мікрофлори не виявили лише в 44,8% спостережень. Поряд з метаплазією слизової оболонки бронхів у ряду досліджуваних хворих визначали диспластичні зміни бронхіального епітелію різного ступеня вираженості. Самостійна ендоскопічна бронхосанація приводила до достовірного зниження загальної частоти дисплазії епітелію бронхів у хворих до 36,1%, у поєднанні зі стандартною протизапальною терапією – до 42,4%.

Висновки. Застосування ендоскопічної фотодинамічної бронхосанації за запропонованою методикою в передопераційному періоді у хворих з метою корекції супутнього ендобронхіту як самостійної, так і в поєднанні зі стандартною протизапальною терапією приводить до зменшення частоти ендобронхіальних ускладнень після оперативного лікування раку легенів у порівнянні з контрольною групою. Ендоскопічна бронхосанація супроводжується значним зниженням вираженості ендоскопічних ознак супутнього ендобронхіту і поліпшенням мукоциліарного транспорту. За даними мікробіологічних тестів у 87 – 88% хворих спостерігали повну санацію бронхіального дерева та зникнення основних гістологічних критеріїв запалення, у 67,2 – 100% хворих – відновлення нормальної будови слизової оболонки бронхіального дерева.

Ключові слова: передопераційна підготовка; ендоскопічна фотодинамічна терапія; післяопераційні ускладнення.

Abstract

Objective. Efficacy of endoscopic bronchosanation for prophylaxis of preoperative and postoperative complications in patients with pulmonary tumors.

Materials and methods. There was studied the efficacy of endoscopic photodynamic therapy in accordance to procedure, elaborated by the authors, including injection of the water solution of a methylene blue dye in concentration 0.04% into tracheobronchial tree, irradiated by laser with the wave length 0.63 mcm, independently and in conjunction with a standard anti–inflammatory therapy as preoperative preparation of tracheobronchial tree in patients, suffering pulmonary cancer. In the investigation 181 patients were included, suffering pulmonary cancer Stages II–III, morphologically confirmed, and with coexistent endobronchitis.

Results. In accordance to analysis of the pathogenic microflora titer and character in lumen of bronchial tree after preoperative preparation there was established, that while application of independent endoscopic bronchosanation in 55 (87%) observations the pathogenic microflora was absent. While combination of photodynamical bronchosanation in accordance to standard therapy a pathogenic microflora was not revealed in 52 patients. While conduction of a standard preparation without application of a laser therapy microflora was not revealed only in 44.8% observations. Together with the bronchial mucosa metaplasia in some investigated patients the dysplastic changes of bronchial epithelium of various severity degree were registered. Independent endoscopic bronchosanation have leaded to trustworthy lowering of a general rate of the bronchial epithelial dysplasia in the patients to 36.1%, together with standard anti–inflammatory therapy – to 42.4%.

Conclusion. Application of endoscopic photodynamic bronchosanation in accordance to the proposed procedure in preoperative period in the patients with objective to correct a concomitant endobronchitis, as independent option or together with standard anti–inflammatory therapy, leads to reduction of the endobronchial complications rate after operative treatment for pulmonary cancer, comparing with a control group. Endoscopic bronchosanation is accompanied by significant lowering of severity of endoscopic signs of coexistent endobronchitits and improvement of mucociliary transport. In accordance to microbiological tests in 87 – 88% of patients a complete sanation of bronchial tree and elimination of main histological criteria of inflammation were noted, while in 67.2 – 100% patients – restoration of normal structure of the bronchial tree mucosa.

Keywords: preoperative preparation; endoscopic photodynamic therapy; postoperative complications.

Introduction

Endoscopic bronchial sanation is widely used to prevent pre– and postoperative complications in patients who have been operated on account of the tumors of the lungs [1, 2]. Surgical treatment of lung tumors differs by the volume of surgical intervention and traumaticity [3]. The causes of complications from the respiratory system are disturbances of microcirculation, lungs drainage [4]. Violation of microcirculation contributes to the development of hypoxia, which is complicated by the presence of pathological content inside the bronchial tree, as well as the presence of an infectious agent [5, 6]. Struggle against postoperative complications requires a lot of efforts and requires a lot of material costs.

Bronchopleural complications of lung cancer surgical treatment are the most severe and dangerous. They include the failure of bronchial stump, bronchial fistula with the development of empyema of the pleural cavity, diffuse purulent endoboronitis [3, 4].

According to various authors, the complications present 3–12% in the general structure of postoperative complications [7]. Postoperative mortality among patients with bronchial fistulas is noted in 21–30% of cases [5].

Inflammatory process in the mucous membrane of the bronchial tree is usually accompanied by edema and hyperemia, decreased elasticity, contact bleeding and the presence of sputum in the lumen of the bronchial tree. In this case, the deterioration of the flashing epithelium drainage function happens, with a violation of microcirculation and the accumulation of thick bronchial secretion [2].

It is generally acknowledged that the state of the bronchial epithelium in the preoperative period in oncological patients is crucial for the course of regenerative processes in the bronchial cultures. Therefore, at present, the success in the treatment of chronic bronchitis is determined by the search for new therapies, including those whose action is aimed at stimulating of regenerative processes [8].

One of them is the method of low–intensity laser irradiation, which is widely used in general clinical practice. But in thoracic surgery, it is used with caution, due to the fact that the mechanism of action and its effect on tumor cells have not been completely studied [6, 8].

From the series of experimental and clinical studies, it is shown that low intensity laser radiation of the red part of the spectrum (λ = 0.63–0.66 μm) provides not only the expressed anti–inflammatory effect and stimulation of tissue regeneration, but also does not stimulate tumor growth [9].

However, in the available literature, there is practically no work on the application and evaluation of the effectiveness of photodynamic therapy as a method of preoperative preparation of the bronchial tree and the treatment of postoperative endobronchial complications in patients after thoracic interventions.

Materials and methods

The study of the effectiveness of endoscopic photodynamic therapy according to the technique developed by us has been performed, with the introduction of an aqueous 0.04% solution of methylene blue dye into the tracheobronchial tree, followed by irradiation of this solution by laser radiation with a wavelength of 0.63 μm along and in combination with the traditional anti–inflammatory therapy, as a preoperative preparation of tracheo–bronchial tree in patients with lung cancer. The study included 181 patients with lung cancer of 2^{nd}–3^{rd} stages, with a morphologically confirmed diagnosis and concomitant endobronchitis.

In the preoperative period, all patients were divided into 3 representative groups. Patients who received preoperative endoscopic photodynamic therapy (63 patients) formed group I, and patients who received comprehensive treatment – endoscopic bronchodilator therapy in combination with conventional anti–inflammatory therapy – were include into group II (60 patients). The third group consisted of patients who received only traditional anti–inflammatory therapy in the preoperative period (58 persons).

The studied groups were standard by the the main prognostic criteria: gender, age, stage of cancer and localization of the tumor process, as well as the severity of the clinical, endoscopic signs of concomitant endobronchitis and the source composition of the microflora of the bronchial tree.

Endoscopic endobronchial rehabilitation was carried out using low intensity radiated red part of the spectrum (λ = 0.63–0.66 μm), in pulsed mode, with a power of 12 mW. Sessions were conducted every other day, patients received 3–6 sessions of bronchosanation.

Objective. Determination of the effectiveness of endoscopic bronchial sanation to prevent pre– and postoperative complications in patients who have been operated on account of the tumors of the lungs

Results

After the completion of the preoperative training with the use of various methods of tracheal–bronchial tree healing, significant changes in the inflammatory process in the bronchial tree, in a series of clinical and laboratory, endoscopic and morphological criteria were noted.

Improvement of general well–being and reduction of the main clinical symptoms of concomitant chronic bronchitis in all studied groups were noted. At the same time, at 3–5 days after the start of preoperative preparation after 1–2 sessions of endoscopic bronchodilator therapy, patients improved their general health, reduced the amount of sputum and changed its character from mucus–purulent to the mucous. In patients of the comparison group, these changes in the clinical manifestations of bronchitis were recorded at a later date, after 10–14 days from the start of treatment. To completely eliminate the clinical phenomena of endobronchitis, 5–6 sessions of pre–operative endoscopic bronchosanation should be performed.

After the completion of the preoperative preparation, it was noted that cough and dyspnea in patients who received endoscopic sanation separately were preserved in 12.7% and 6.3% of cases, respectively (*table 1*). When conducting complex preoperative preparation, before the treatment the cough and dyspnoea were observed in 96.6% and 63.3% of patients respectively. After treatment, these symptoms were preserved in 8.3 % and 6.7% of patients, respectively. In the control group, after preoperative preparation, cough was

Table 1. **Intensity of clinical signs of endobronchitis in the preoperative period**

Clinical symptoms	Bronchosanation		Bronchosanation and traditional methodics		Traditional methodics	
	before the treatment	after the treatment	before the treatment	after the treatment	before the treatment	after the treatment
Cough, %	85.7	12.7	96.6	8.3	100	34.5
Fever, %	60.3	12.7	70.0	10.0	75.8	21.4
Dyspnea, %	50.7	6.3	63.3	6.7	60.0	31.3

Table 2. **Intensity of endoscopic signs of endobronchitis in the preoperative period**

Endoscopic signs	Bronchosanation		Bronchosanation and traditional methodics		Traditional methodics	
	before the treatment	after the treatment	before the treatment	after the treatment	before the treatment	after the treatment
Hyperemia of mucous membrane, %	90.4	7.9	96.6	3.3	96.6	26.5
Swelling of mucous membrane, %	71.6	3.2	85.0	–	86.2	20.6
Sputum presence, %	79.0	4.7	81.6	1.6	79.6	24.1

Table 3. **Histological signs of endobronchitis in the preoperative period**

Histological signs	Bronchosanation		Bronchosanation and traditional methodics		Traditional methodics	
	before the treatment	after the treatment	before the treatment	after the treatment	before the treatment	after the treatment
Fibrosis, %	93.1	48.8	91.6	47.2	93.3	86.7
Metaplasia, %	83.7	–	86.1	–	86.6	46.7
Leukocytes accumulation, %	79.1	–	83.3	–	86.6	40.0
Swelling of mucous membrane, %	81.3	–	80.5	–	76.6	40.0
Lymphoid infiltration, %	65.1	32.6	61.1	27.8	53.3	33.3
Hyperplasia of glands, %	30.2	4.7	30.5	–	46.6	26.7

observed in 20 patients (34.5%), dyspnea – in 18 patients (31.3%). Differences in the groups are statistically significant ($p < 0.05$).

At the end of the course of preoperative preparation marked significant changes in the endoscopic pattern of the bronchial tree were noted. After endoscopic laser therapy independently, the hyperemia of the mucous membrane of the bronchi remained only in 7.9 % of patients, swelling of the bronchial mucosa – in 3.3%, and the presence of sputum in the lumen of the bronchial tree was observed only in 4.7% of cases. In the group of combined preoperative preparation, the results of the performed treatment are even more effective – the swelling of the mucous membrane accompanied by the presence of sputum in the lumen of the bronchial tree was retained only in one patient (1.6%) and mucosal hyperemia was observed in 3.3 % of cases (*table 2*).

During preoperative preparation with the use of traditional anti–inflammatory therapy, none of the endoscopic signs of inflammation were completely compensated, but they were just slightly decreased in their number.

After treatment, the hyperemia of the bronchi mucous membrane was observed in 27.5% of cases, edema of the mucous membrane at 20.6%, sputum in the lumen of the bronchial tree was noted in 24.1% of cases.

In the analysis of the titre and the nature of the pathogenic microflora in the lumen of the bronchial tree after the preoperative preparation, it was found that in the application of endoscopic bronchoconstriction independently, in 55 (87%) of the cases the pathogenic microflora were absent. When combined photodynamic bronchosanation with traditional therapy, pathogenic microflora was not detected in 52 patients. In the group of traditional preparation without the use of laser therapy, the absence of microflora was noted only in 44.8%. The difference is statistically significant ($p < 0.05$).

In analyzing the results of preoperative preparation, it was noted that better indicators were detected in patients from the group where the combination of endoscopic bronchosantation and traditional drug correction was used. A slight difference in the positive effect of this method of preoperative preparation, compared with a group of patients who received endoscopic laser sanation in an independent form, is probably due to the short use of traditional therapeutic agents within 10–14 days.

The rapid and pronounced rehabilitation effect of endoscopic photodynamic therapy was confirmed in the calculation of the severity index of bronchitis, which is a mathematical method for evaluating the effectiveness of the treatment.

In the study, the dynamics of the severity index clearly demonstrated the regression of almost all clinical and laboratory signs of concomitant chronic bronchitis in patients with lung cancer for 10–14 days from the beginning of preoperative preparation, with the use of endoscopic laser therapy.

Another objective method for assessing the effectiveness of the preoperative preparation was the determination of the rate of mucociliary clearance (MCC), since in a long inflammatory process (like in chronic endobronchitis) there is always a significant decrease in the drainage function of the bronchi. The used therapeutic agents, which make up the complex of traditional anti–inflammatory therapy, cause only slight increase in mucociliary clearance to 30%. After the preoperative preparation with the use of endoscopic bronchosanation according to the proposed method, it was found that the MCC rate has increased significantly and is equal to 45–50%, which corresponds to the normal rate of MCC.

Endoscopic photodynamic bronchodilator therapy according to the histological study contributed not only to the decrease of a number of morphological manifestations of chronic inflammation, but also to the normalization of the structure of the mucous membrane of the bronchi, with the restoration of cilia of the flashing epithelium. It is further connected with the fact that the basis of the effect of the proposed method of bronchosanatio there is the stimulation of regenerative processes characterized by the structural and functional value of the newly created tissue, the restoration of its organospecificity.

In the microscopic examination of histological samples of the mucous membrane of the bronchi, it was noted that after the preoperative endoscopic bronchodilator therapy, the swelling of the mucous membrane and leukocytes in the cluster were completely absent, whereas in patients of the control group these signs were preserved in 40.0 % of cases (*table 3*).

The complete regression of the bronchial epithelium metaplasia, with the restoration of the mucous membrane normal structure in patients from I and II groups was noted. In the control group, the metaplasia of the epithelium, which characterizes the inflammatory process in the bronchial system, remained in 46.7 % of cases. The intensity of other signs of inflammation in the bronchial tree was significantly lowered under the influence of endoscopic bronchosanation compared with the control group ($p<0.05$).

Along with the metaplasia of the mucous membrane of the bronchi, a number of patients of the studied groups showed the dysplastic changes of the bronchial epithelium of different degrees of severity. Under the action of endoscopic bronchosanation, there is a significant reduction in the total number of bronchial epithelial dysplasia in patients of groups I and II, to 36.1 % and 42.4 %, respectively.

It should be emphasized that this effect is observed due to the complete relief of I and II degrees dysplasia and the transition of grade III dysplasia to dysplasia of a mild degree of severity.

Discussion

In patients who received the traditional preoperative preparation, dysplastic changes in the bronchial mucosa remained in over 75% of the cases, with more than half of the cases following the treatment, the initial degree of dysplasia was observed.

In the group of patients who received endoscopic photodynamic bronchosanation with the introduction of aqueous solution of methylene blue into the tracheobronchial tree in combination with traditional preoperative preparation, endobronchial complications after surgical treatment were recorded only in 12.1% of cases. In 3 cases the bronchial fistulas developed, in one – the diffuse endobronchitis.

Complications in patients receiving anti–inflammatory therapy without additional bronchusation were noted in 9 cases, which was 31.3%. In 6 patients, there was a bronchial fistula, in 3 – endobronchitis of II–III degrees of severity.

Conclusions

Thus, the use of endoscopic photodynamic bronchoscopy according to the proposed method in the preoperative period in patients with a view to correcting concomitant endobronchitis, both along and in combination with traditional anti–inflammatory therapy, leads to a decrease in the number of endobronchial complications in the surgical treatment of lung cancer, as compared to the control group.

Under the action of endoscopic bronchoconstriction there is a pronounced reduction of endoscopic signs of concomitant endobronchitis and improvement of mucociliary transport. According to microbiological tests, in 87–88% of cases there is complete rehabilitation of the bronchial tree and elimination of the basic histological criteria of inflammation and in 67.2–100.0% of cases – marked restoration of the normal structure of the mucous membrane of the bronchial tree.

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