Polymorbidity in Inflammatory Bowel Diseases

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Peculiarities of the electromotor activity of the small intestine and ascending and descending portions of the colon were revealed in patients with inflammatory bowel diseases associated with bronchopulmonary system dysfunction. Functional test revealed an increase in the vital capacity of the lungs due to increased patency of small bronchi.

Key Words: *bronchopulmonary diseases; inflammatory bowel disease; polymorbidity*

Inflammatory bowel diseases (IBD) are often accompanied by manifestations of bronchopulmonary pathology. According to different authors, extraintestinal or systemic manifestations of IBD are observed in 5-55% patients with this pathology [5-7]. About 80% patients with lung pathology have IBD [8]; it should be noted that IBD developed more often in all respiratory diseases except bronchial asthma.

Common parasympathetic innervation of lungs, ascending colon, and a portion of transverse colon with the vagus nerve can play a role in the pathogenesis of bronchopulmonary manifestations associated with IBD. The vagus nerve is considered to be the major regulator of respiratory function. Its pre- and postganglionic fibers are cholinergic [2]. Cholinergic innervation induced contraction of airway smooth muscles and gland secretion. Efferent vagal fibers regulate bronchial patency and increase the tone of smooth muscles, which determines the velocity and volume of air entering the lungs [1]. Cholinergic innervation enhances motor and secretory functions of the gut. More than 70% fibers in the vagus nerve are afferent; in IBD, they carry pathologically changed afferent impulses to the vagal bulbar centers, which leads to changes in alveolar epithelium permeability and production of autoantibodies to own cell proteins, e.g. antilymphocyte antibodies, and circulating immune complexes [12].

Pleurisy, respiratory diseases, interstitial lung diseases, pulmonary eosinophilia, thromboembolic diseases, vasculites, granulomatous pulmonary conditions, *etc.* are reported among IBD-associated lung diseases [10,11]. Bronchiectases as systemic manifestations of IBD are rare. Pulmonary manifestations of IBD, *e.g.* interstitial pulmonary fibrosis, are also observed in children [9]. Increased activity of cholinergic system followed by restrictive and obstructive lung disorders can play a role in the mechanisms underlying the development of combined successive pathological processes in the colon and the lungs. In embryogenesis, the lungs and mucosa of the digestive tube have common origin and are formed from the same endodermal leaflet; therefore, the lungs are easily involved into the pathologica process in IBD.

Here we studied peculiarities of motor activity of the small and large intestines in IBD associated with bronchopulmonary pathology.

MATERIALS AND METHODS

Electromotor activity (EMA) was recorded with silver cutaneous electrodes (contact surface area 0.5-0.6 mm^2) placed on the anterior abdominal wall above the intestine, ascending colon, and descending colon projections. The signals were recorded for 15-20 min with preamplification using a Conan-M hardware/software complex with a bandwidth from 0.01 Hz to 10 kHz and a noise level <1-5 μV. The characteristics of slow wave and spike activity (amplitude and frequency) were measured on the electromyographic curve.

Respiratory function was assessed on an Eton pneumotachometer by recording spirographic curve

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forced expiration flow—volume curve. The test was performed in the sitting position on an empty stomach or 2 hours after meal in the morning by the standard method. The following parameters were analyzed: vital lung capacity, forced expiration volume over 1 second (FEV_1), peak expiratory flow rate, maximum flow rate (MEFR) at 25, 50, and 75% of forced vital capacity ($MEFR_{25}$, $MEFR_{50}$, and $MEFR_{75}$, respectively).

Reduced FEV_1 indicated impairment of pulmonary ventilation capacity; reduced vital lung capacity pointed to restrictive ventilation disorders; reduced FEV_1 and velocity parameters of the forced expiratory flow—volume loop ($MEFR_{25}$, $MEFR_{50}$, and $MEFR_{75}$) were considered to be the signs of obstructive ventilation disorders. By conventional criteria, reduced velocity parameters indicate generalized airway obstruction; decreased peak expiratory flow volume and $MEFR_{25}$ attest to obstruction of the large bronchi; decreased $MEFR_{50}$ and $MEFR_{75}$ or only $MEFR_{75}$ attest to obstruction of the small bronchi. Standard bronchodilator test was performed using salbutamol, a β_2-adrenergic receptor agonist.

The study included 57 patients at the age of 26-64 years (mean age 38.0±4.5 years) with ulcerative colitis and Crohn's disease; of them 35 patients had IBD-associated airway disease and 22 had isolated IBD.

Statistical analysis was performed using Statistica 6.0 software, confidence intervals at $p<0.05$ were calculated.

RESULTS

IBD manifestations were pain in the projection of the colon and diarrhea with mucus and blood. The mean history of IBD was 9.8±3.5 years (3-15 years). Bronchopulmonary pathology was regarded as a manifestation of polymorbidity in IBD.

Parameters of the respiratory function in patients with IBD before and after the pharmacological test with salbutamol are presented (Fig. 1; Table 1).

Reduced $MEFR_{50}$ and $MEFR_{75}$ on the flow—volume curve (Fig. 1) attested to impaired bronchial patency at the level of small bronchi.

Vital lung capacity in patients with IBD was reduced (Fig. 1); β_2-receptor agonist salbutamol increased FEV_1 (5.1%), which demonstrates the resolution of bronchospasm after β_2-adrenoceptor activation. Functional test with salbutamol showed that MEFR at the level of major bronchi increased by 21.6% and at the level of small bronchi by 35.8%. Thus, bronchial patency improved primarily due to increased flow rate at the level of small bronchi, which suggests functional mechanisms are possibly involved in the development of obstructive symptoms.

At the same time, EMA of the small intestine as well as of ascending colon and descending colon were evaluated.

In patients with IBD associated with bronchopulmonary pathology, the frequency of EMA slow waves in the intestine was 9.9±0.8 spikes per min (below the normal by 45%, $p<0.05$); amplitude, 0.12±0.03 mV (below the normal by 40%, $p<0.05$). Low-amplitude spike activity with a frequency of 0.76±0.04 spikes per min and amplitude of 0.07±0.02 mV was registered (Fig. 1).

In patients with isolated IBD, the frequency of EMA slow waves in the intestine was higher than in patients with IBD associated with bronchopulmonary pathology: 11.4±1.8 spikes per min (below the normal by 36.7%, $p<0.05$); amplitude, 0.14±0.03 mV (below the normal by 30%, $p<0.05$). Low-amplitude spike activity with a frequency of 1.06±0.04 spikes per min and amplitude of 0.065±0.005 mV was detected.

Thus, respiratory involvement in IBD is accompanied by more pronounced EMA changes in the intestine than in patients with isolated IBD.

In patients with IBD associated with bronchopulmonary pathology, the frequency of EMA slow waves in the ascending colon was 9.4±0.8 spikes per min (below the normal by 37.5%); amplitude, 0.13±0.02 mV (below the normal by 35%, $p<0.05$). Low-amplitude spike activity with a frequency of 1.13±0.03 and amplitude of 0.070±0.002 mV (Fig. 2, *a*) was noted.

In patients with isolated IBD, the frequency of EMA slow waves in the ascending colon was higher than in patients with IBD associated with bronchopulmonary pathology: 11.3±1.4 spikes per min (below the normal by 24.7%, $p<0.05$); amplitude, 0.16±0.03 mV (below the normal by 20%, $p<0.05$). Low-amplitude spike activity with a frequency of 1.24±0.14 spikes per min and amplitude of 0.065±0.005 mV were recorded.

TABLE 1. Dynamics of Functional Parameters of the Lungs in Patients with IBD before and after Pharmacological Test with Salbutamol

Time	VLC	FEV_1	PEF	$MEFR_{25}$	$MEFR_{50}$	$MEFR_{75}$
Baseline vales	3.36±0.64	2.77±0.45	6.37±1.50	5.26±0.90	3.24±0.65	0.95±0.30
After salbutamol test	3.47±0.74	2.91±0.60	6.08±1.20	6.4±1.5	3.73±0.70	1.29±0.34

Note. VLC: vital lung capacity, PFR, peak expiratory flow.

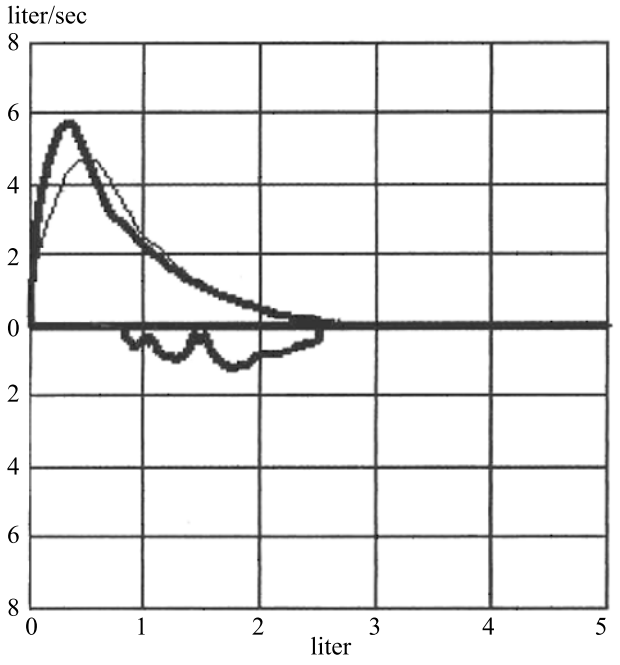

Fig. 1. Patient E. Decrease in pulmonary ventilation capacity, severe bronchial obstruction.

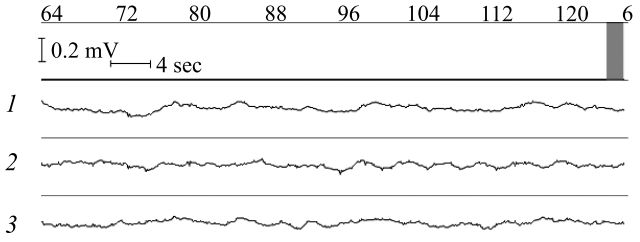

Fig. 2. Patient A. with IBD-associated lung disease. EMA of small intestine (*1*), ascending colon (*2*), and descending colon (*3*).

Hence, IBD-associated lung involvement was accompanied by more pronounced decrease in EMA in the ascending colon in comparison to that in patients with isolated IBD.

In patients with IBD associated with bronchopulmonary pathology, the frequency of EMA slow waves in the descending colon was 9.80±0.07 spikes per min (surpassed the normal by 63.6%); amplitude, 0.16±0.02 mV (below the normal by 25%, $p<0.05$). Low-amplitude spike activity with a frequency of 1.4± 0.2 spikes per min and amplitude of 0.080±0.002 mV were recorded (Fig. 2, *б*).

In patients with isolated IBD, the frequency of EMA slow waves in the descending colon was higher than in patients with IBD associated with bronchopulmonary pathology: 11.2±1.3 spikes per min (above the normal by 85.8%, $p<0.05$); amplitude, 0.14±0.02 mV (below the normal by 30%, $p<0.05$). Low-amplitude spike activity with a frequency of 1.3±0.2 spikes per min and amplitude of 0.08±0.01 mV did not differ from the previous group.

Pulmonary involvement in IBD is accompanied by a more pronounced decrease in EMA in the descending colon than in patients with isolated IBD. Activation of the efferent vagal neuronal signaling pathway can inhibit the release of cytokines, thus protecting the tissues from cytokine damage (the cholinergic anti-inflammatory signaling pathway) [3].

The results of our study suggest that respiratory involvement in IBD leads to more pronounced inhibition of slow-wave motor activity of the small and large intestine. This apparently indicates the development of reflex responses with participation of the vagus nerve innervating the respiratory system and the ascending colon and its various efferent fibers, *e.g.* purinergic. The increase in airway patency during activation of β_2-adrenoceptors in combined pathology attests to interactions of autonomic nervous system components during regulation of motor activity in both the small and large intestine and bronchopulmonary system.

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