

main therapeutic and prophylactic method in AO allows to preserve and sometimes to restore reproductive function in almost 4 of 5 women with AO and reduce the rate of AO and CHFO relapse development.

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OESOPHAGEAL ACHALASIA TREATMENT EFFICACY BY THE METHOD OF ENDOSCOPIC INTRODUCTION OF THE BOTULINIC TOXIN

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ЭФФЕКТИВНОСТЬ ЛЕЧЕНИЯ АХАЛАЗИИ КАРДИИ МЕТОДОМ ЭНДОСКОПИЧЕСКОГО ВВЕДЕНИЯ БОТУЛИНИЧЕСКОГО ТОКСИНА

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Баллонная дилатация нижнего пищеводного сфинктера баллонами диаметром 30–40 мм или введение ботулинического токсина в этой области являются эффективными методами, которые позволяют устранить проявления дисфагии в течение 3–12 мес. Цель — изучить воздействие ботулинического токсина на давление нижнего пищеводного сфинктера и разработать прогностические критерии эффективности терапии ботулиническим токсином. В исследование были включены 32 пациента (22 мужчин, 10 женщин) с 1-й и 2-й стадиями ахалазии, которым проводили эндоскопи-



ческие инъекции ботулинического токсина типа А в области нижнего пищеводного сфинктера (препарат Диспорт). Было установлено, что давление нижнего пищеводного сфинктера и эвакуация бария из пищевода в первый день после этой инъекции являются важным прогностическим индикатором эффективности. Пациентам с хорошим ответом на введение ботулинического токсина лечение должно быть продолжено, а у пациентов с плохим ответом после возобновления симптомов необходимо выполнение кардиомиотомии. Актуальны широкое внедрение оптимизированной терапии ботулиническим токсином в клиническую практику и разработка схем проведения малоинвазивных эндоскопических процедур и показаний к их применению в лечении ахалазии пищевода.

Ключевые слова: ахалазия пищевода, инъекция ботулинического токсина.

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ESOPHAGEAL ACHALASIA TREATMENT EFFICACY BY THE METHOD OF ENDOSCOPIC INTRODUCTION OF THE BOTULINIC TOXIN

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Background. Lower esophageal sphincter (LES) balloons dilation with a diameter of 30–40 mm or the introduction of botulinum toxin in this area are more efficient methods that allow to remove manifestations of dysphagia during the period from 3 to 12 months. However, after the expiration period the therapy sessions should be repeated or surgical treatment with the performance of cardiomyotomy should be performed.

The aim was studying effectiveness of botulinum toxin on the performance of pressure in the NPC to develop prognostic criteria for botulinum toxin therapy effectiveness.

Methods. The study included 32 patients (22 men, 10 women) with the 1st and early 2nd stage of AK, which were treated by endoscopic injections of botulinum toxin type A in the area of NPC (the drug Dysport, MO 500/3 mb.)

Results. Analysis of symptoms and level of pressure in the cardia showed no correlation between them and the stage of achalasia. A higher rate of transient relaxations of esophageal-gastric junction in comparison occurred at the 1st and early 2nd stage of achalasia cardia (AC) with later stages. Response to therapy is to reduce the pressure in the cardia, the restoration of peristaltic function of the esophagus, reducing the time delay of barium in the esophagus, which correlated with a decrease in severity of symptoms.

Conclusions. The pressure in the cardia and the evacuation of barium from the esophagus on the first day after injection of botulinum toxin is an important prognostic indicator of the effectiveness of its patients with AC. Patients with good response to the introduction of botulinum toxin treatment should be continued, and in patients with poor response after the resumption of symptoms cardiomyotomy will be performed. Widespread introduction of suitable botulinum toxin therapy in clinical practice, development schemes of performing minimally invasive endoscopic procedures and indications for their use in the treatment of achalasia of the esophagus.

Key words: oesophageal achalasia, botulin toxin injection.

Background

Achalasia cardiae (AC) is idiopathic disease characterized by lack of response of relaxation of the lower esophageal sphincter (LES) in response to swallowing, caused by an imbalance between excitatory (acetylcholin containing or containing substance P) and inhibitory (containing vasoactive intestinal peptide or nitric oxide) neurons as a result of selective loss of inhibitory nerves [1]. Patients with AC revealed degenerative changes in the intramuscular plexus LES [2] and a pronounced decrease in activity of nitric oxide synthesis [3]. Patients with AC noted dysphagia, chest pain, weight loss. The disease has two peaks of age of manifestation — 20–30 and 50–60. The aim of treatment is to reduce the AC pressure pump station and restore its ability to relax. At early stages of the

disease can be a temporary effect of intake of nitrates and calcium channel blockers. At present, medical treatment of AC is considered ineffective.

NPC balloons dilation with a diameter of 30–40 mm or the introduction of botulinum toxin in this area are more efficient methods that allow to remove manifestations of dysphagia during the period from 3 to 12 months. However, after the expiration period the therapy sessions should be repeated or surgical treatment with the performance of cardiomyotomy [4]. One of the measurements of the effectiveness of the treatment is to reduce the pressure in the pump station and restore its ability to relax.

The Aim of the Study

To study the effectiveness of botulinum toxin on the performance of pressure in the LES to

develop prognostic criteria for the effectiveness of botulinum toxin therapy.

Material and Methods

The study included 32 patients (22 men, 10 women) with the 1st and early 2nd stage of AC, which were treated by endoscopic injections of botulinum toxin type A in the area of LES (the drug Dysport, MO 500/3 mb.). Men's age was 24–69, women's — 20–68 years old.

Medical procedure was performed as follows. Esophagoscopy was performed under local anesthesia. Observing the rules of antisepsis four injections of the drug Dysport were performed. Piercing the mucosa, the drug was injected into the pump station at points corresponding to 3, 6, 9, and 12 hours. At each point it was injected 60 units of the drug. The total dose should not exceed 250 units. Complica-



Table 1

Monometric Value of Intraoperative Patients

Value	Stage		
	1	1-2	2
Pressure in cardia, mm Hg.	38.6±12.5	45.2±14.4	56.4±12.3
The frequency of cardia relaxation, the hour	2.1±1.2	1.60±0.81*	0.80±0.35*

Note. * — differences were statistically significant ($d < 0,05$).

Table 2

Effectiveness of Botulinum Toxin Therapy in Patients with Achalasia

Effectiveness value	Before introduction of toxin, n=32	After introduction of toxin, n=32
The delay of contrast in the esophagus, sec	364±124	32.0±24.1*
Pressure in cardia, mm Hg	58.6±15.4	13.68±8.90*
Esophageal peristalsis, mm Hg	24.0±15.6	34.0±12.4*
Dysphagia, scores	5.6±2.4	1.4±0.7*
Chest pain, scores	5.3±2.4	2.1±1.2*
Regurgitation, scores	4.2±1.4	1.8±0.8*
Weight lost, %	9.2±2.2	0.7±1.2*

Note. * — differences are scientifically significant ($d < 0,05$).

tions associated with intervention and/or the introduction of the toxin were observed. All patients underwent a comprehensive survey: endoscopy, barium suspension roentgen tests with the definition of the delay time of barium in the esophagus, esophageal manometry with the definition of pressure in the NPS.

After the introduction of botulinum toxin on the 1st and 7th day, the pressure was measured in the NPC, as well as determination of the time delay of barium suspension in the esophagus. Patients were examined 1 month after the procedure, then at intervals of 3 months from the time of drug administration for 1.5 years (the study of pressure in the pump station, the definition of consistency of esophageal peristalsis, X-ray examination with the definition of esophageal emptying time, the analysis of clinical presentations with visual analogue scale of severity of dysphagia with a maximum estimate of 10 points). Statistical analysis of the results was performed using standard statistical tests; data processing was carried out in the program Microsoft Excel XP.

Results and Discussion

Analysis of symptoms and level of pressure in the cardia showed no correlation between them and the stage of achalasia. But at the 1st and early 2nd stage of AC occurred a higher rate of transient relaxations of esophageal-gastric junction in comparison with later stages (Table 1). Response to therapy is to reduce the pressure in the cardia, the restoration of peristaltic function of the esophagus, reducing the time delay of barium in the esophagus, which correlated with a decrease in severity of symptoms (Table 2).

The pressure level in NPC correlated with the time of the evacuation of the esophagus (Spearman correlation coeffi-

cient — 0.85, $p < 0.05$). Noted the almost linear relationship between the indicators of pressure in the pump station on the 1st and 7th day after surgery, so for further calculations, we used data from manometry and roentgen tests on the 1st day after surgery.

In the analysis of long-term results were divided into three groups. The first — with the pressure in the cardia after injection

of botulinum toxin less than 10 mm Hg, the second — 10–20 mm Hg, the third — more than 20 mm Hg. Results of monitoring patients after treatment are shown on Fig. 1. Differences in the results indicate the possibility of using pressure levels after administration of botulinum toxin as a prognostic criterion of its effectiveness.

The relation between the level of pressure in achalasia car-

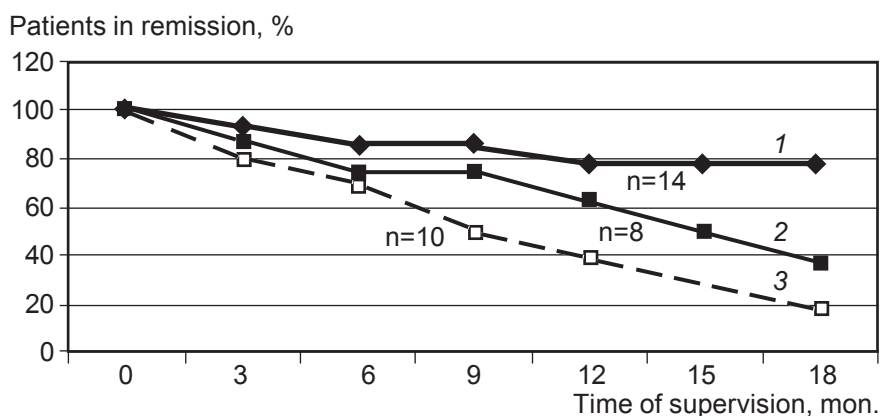


Fig. 1. The probability of recurrence of symptoms, depending on the pressure in the gastric cardia after injection of botulinum toxin. Differences between groups are scientifically significant ($d < 0,05$): 1 — < 10 mm Hg; 2 — 10–20 mm Hg; 3 — > 20 mm Hg



Table 3

The Relationship between the Pressure after the Administration of Botulinum Toxin and the Clinical and Manometric Parameters at 1 and 18 Months

Effectiveness scores, condition	Complex survey	Pressure in the NPS after the introduction of botulinum toxin, mm Hg		
		< 10, n=27	10–20, n=22	> 20, n=16
Pressure in NPS, mm Hg				
beyond remission	1	7.5±3.6	14.0±7.5	24.0±15.6
remission	18	12.4±8.6	24.0±15.6	24.0±15.6
recurrence	18	32.1±15.6	44.0±15.6	56.1±18.6
Integral assessment of symptoms, scores				
beyond remission	1	1.6±1.1	1.8±1.4	2.1±1.2
remission	18	1.23±1.20	1.6±1.1	2.2±1.6
recurrence	18	3.6±2.1	4.8±1.8	5.4±2.4
Weight loss, %				
beyond remission	1	0.71±1.10	0.83±1.20	0.57±1.40
remission	18	0.58±0.21	0.67±0.23	0.71±1.10
recurrence	18	4.2±2.2	9.7±2.2	10.4±2.2

dia after relapse and severity of symptoms (Table 3). Also, the level of pressure of field injection of botulinum toxin has been associated with the intensity of the return of symptoms and the level of pressure in the pump station after the recurrence of achalasia. According to modern concepts, the method of choice for early treatment of AC is the introduction of botulinum toxin in the area of NPC or balloon dilatation. Several studies have shown that the best results compared to these methods which allows early surgical treatment [5]. However, in our opinion, the use of endoscopic techniques is justified with proper patient selection.

Our observations show that patients with good response to therapy with botulinum toxin, which is characterized by a decrease in pressure in the pumping station is less than 10 mm Hg on the first day after injection, decreasing the time delay of barium to normal values and a decrease in the severity of symptoms until the complete regression of dysphagia, it is possible

to predict the effectiveness of treatment is not inferior to operative procedures [6], but with the advantage of minimally invasive and convenience for patients. Also, there is no doubt about the advantage of using botulinum toxin in elderly and senile patients, in patients with severe concomitant diseases, and patients who refuse surgery.

Conclusions and Prospects for Further Research

The pressure in the cardia and evacuation of barium from the esophagus on the first day after injection of botulinum toxin is an important prognostic indicator of the effectiveness of its patients with achalasia cardia.

Patients with good response to the introduction of botulinum toxin treatment should be continued, and in patients with poor response after the resumption of symptoms cardiomyotomy will be performed.

Widespread introduction of suitable botulinum toxin therapy in clinical practice, development schemes of performing of minimally invasive endoscopic pro-

cedures and indications for their use in the treatment of esophageal achalasia.

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