The Treatment of Achalasia by Injection of Botulinum Toxin Type A under Endoscopic Ultrasound Assistance

Liu Qingsen, Cai Fengchun, Guo Rongbin, Meng Jiangyun, Cheng Liufang, Cheng Fengqi, Li Li

(The General Hospital of PLA, Beijing 100853)

Abstract

To test the hypothesis that injection of botulinum toxin type A under endoscopic ultrasound assistance may effectively reduce the occurrence of spasm at gastric cardia, and to offer an effective treatment for achalasia, 10 patients with achalasia who confirmed by exclusion of secondary causes by routine upper endoscopy and barium meal were enrolled for study. The lower esophageal sphincter (LES) was identified as a thickened hypoechoic zone. A total of four 1 ml injections (80U) of botulinum toxin type A were made in different quadrants of the LES in each patient. A dysphagia score, which was the sum of the individual scores of dysphagia, regurgitation and chest pain, was given to each patient, and LES pressure was measured before and after treatment. The results showed that LES pressure (5.05 ± 11.56 kPa vs 3.36 ± 1.51 kPa) and dysphagia score (6.10 ± 2.02 vs 1.30 ± 1.27) wre decreased significantly (both $P<0.01$) after the treatment. The botulinum toxin injection with the assistance of endoscopic ultrasound appeared to be a very safe, effective and promising alternative for the currently available therapeutic tools for achalasia.

Key words: Esophageal achalasia; Esophagogastoric junction; Botulinum toxin type A; Endosnography

Now it is thought that achalasia is a esophagus power disease, characterized by lack of peristalsis and disturbance in relaxation[1]. Most patients can get positive curative effect for the present therapies, but the risk is high, and there are many complications. The risk of expansion of air sacs accompany perforation was 1% - 5%, and it was generally difficult to maintain long-term effects at once. Generally the 5-year remission rate was 25%, and repeated therapies were usually needed during this time interval[2]. During Nov 1997 – April 1998, we performed botulinum toxin type A (LANTOX) injection under endoscopic ultrasound (EUS) assistance for 10 cases of achalasia patients and obtained successful results.

Material and Method

1. Selection of Cases

10 patients were confirmed as achalasia according to clinical symptoms, esophagus

pressure test, upper alimentary barium meal and endoscopic examination. There were 8 males and 2 females, age ranged from 13 – 64 years, with an average of 36.9 ± 13.4 years. 5 cases used to accept drug therapy, 2 cases processed 2 times of air sac expansion therapy, no obvious effect.

2. Machines and Drugs

Japan Fujinon EG-410HR electronic endoscope system, biopsy passage diameter 2.8mm, application length 1100mm. Japan Fujinon SP-701 endoscopic ultrasonic probe system, probe diameter 2.6mm, application length 2000. U.S. Microvasive adjustable tubing syringe, length 200cm, outer shell diameter 2.3mm. LANTOX produced by Lanzhou Institute of Biological Products.

3. Operations

Before 6 hours of the therapy, the patient could not drink. After routine upper alimentary canal endoscope examination, ultrasonic probe (USP) was applied to examine the thickness of each wall of lower segment of esophagus to ensure that the needle can achieve the proper skin layer of lower esophageal sphincter (LES), and prevent too-shallow or too-deep injection. A vial of 100U LANTOX was diluted to 5 ml by saline, and injected into upper part of zigzag ring from 3, 6, 9, 12 o'clock position, each from 4 points, 20U for each point. After injection, USP examination was processed again. Injection achieved LES indicated the thickening of hypoechoic zone in proper skin layer. After operation, the patients were reminded to take 20mg famotidine twice a day orally. The appearance and disappearance times of adverse effects were recorded. Esophagus power test was processed within a week.

4. Effectiveness Evaluation

Scored before and after a week of therapy for 3 main symptoms: dysphagia, backflow of food and retrosternal pain respectively. The standard was as follows. 0: no symptoms; 1: occasionally; 2: frequently, almost happened everyday; 3: frequently happened in a day, almost each meal. Alimentary canal bedside pressure examination system from U.S. Sandhill Company BioLAB was used. T-test was processed before and after therapy for both examinations.

Results

1. Clinical Effects

The curative effects showed immediately in 9 cases among 10, and the symptoms were obviously improved. The effects achieved the best at 27 – 72hours. There was 1 case with not obvious symptom improvement, but the lower esophageal sphincter

power (LESP) decreased from 4.90kPa before therapy to 3.63 kPa after therapy. The scores of main symptom decreased from 6.10 ± 2.02 before therapy to 1.30 ± 1.27 after therapy ($P<0.01$).

2. LESP Evaluation

The LESP obviously decreased after therapy for 8 patients among 10. Although the reduction was not obvious in the other 2 cases, the symptoms had already improved obviously. The LESP before and after therapy were 5.05 ± 1.56 kPa and 3.36 ± 1.51 kPa ($P<0.01$) respectively.

3. Adverse Effects

Most patients (7 cases) had retrosternal pain or uncomfortable and dull pain of xiphoid process, which generally disappeared within 24 – 72 hours. No obvious uncomfortable reaction and complication happened.

Discussion

BTXA is a protein produced by anaerobic fusiform bacillus botulinum bacteria, the main action mechanism is paralyzing muscle through inhibition of release of acetylcholine from nerve endings. Pasricha *et al*[3-5] had proved in animal and clinical studies that BTXA injection into LES could decrease LES pressure. 21 cases of double blind test proved that the short term effect could achieve 90%, but the effect could maintain for over 6 months in 2/3 patients, and would decrease on an average of 15 – 16 months, but repeated injections were still effective. The reason for the insecurity of the long term effect may be that usually the endoscopic injection could not accurately be located into proper layer, and was just by chance, the injection needle may not achieve or just partially achieve into LES, thus leaded to failure or early recurrence. Injection under endoscopic ultrasound assistance could ensure the injection of BTXA into LES[6], thus maximized inhibition against nerve muscle joint, reduced chance of recurrence. The results indicated that BTXA injection under EUS assistance in treating achalasia is easy, safe and effective, and is specially suitable for patients that cannot endure therapies will cause injury. Its long term effects need to be further observed.

References

1. Singaram C, Sweet MA, belcaster G, *et al.* Detection of a novel antineuronal autoantibody in patients with achalasia. Gastroenterology, 1994, 108: A556.
2. Eckardt VF, Aignherr C, Bemhard G. Predictors of outcome in patients with achalasia with poeumostatic dilatation. Gastroenterology, 1992, 103: 1732.

3. Pasricha PJ, Ravich WJ, Hendrix TR, *et al.* Treatment of achalasia with intrasphincteric injection of botulinum toxin: A pilot trial. Ann Intern Med, 1994, 121: 590.
4. Pasricha PJ, Ravich WJ, Hendrix TR, *et al.* Intrasphincteric botulinum toxin for the treatment of achalasia[J]. N Engl J Med, 1995, 322: 774.
5. Pasricha PJ, Rai R, Ravich WJ, *et al.* Botulinum Toxin for achalasia: long term follow up and predictors of outcome. Gastroenterology, 1996, 110:1410.
6. Deviere J, Dunham F, Richaert F, *et al.* Endoscopic ultrasongraphy in achalasia. Gastroenterology, 1989, 96: 1210.

(Originally published in Medical Journal of Chinese People's Liberation Army, 1999; 24(2): 115)