ORIGINAL ARTICLE

TJG
The Turkish Journal of Gastroenterology

# Double-balloon endoscopy in patients with Peutz-Jeghers syndrome

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***Background/aims:*** *Peutz-Jeghers syndrome is a rare hereditary syndrome characterized by mucocutaneous pigmentation and hamartomatous polyps of the gastrointestinal tract, especially in the small intestine. Double-balloon endoscopy is a new endoscopic technique that enables both endoscopic visualization of the entire small bowel and therapeutic interventions in a single procedure. In this study, we evaluate the efficacy and safety of double-balloon endoscopy for both treatment and surveillance of patients with Peutz-Jeghers syndrome.* ***Materials and Methods:*** *We retrospectively evaluated 7 consecutive patients who were referred to Dokuz Eylül University, Gastroenterology Department, with the diagnosis of Peutz-Jeghers syndrome between 2007 and 2010.* ***Results:*** *Patients with Peutz-Jeghers syndrome (M/F: 5/2) underwent a total 31 double-balloon endoscopy procedures: 21 by the oral route, 9 by the anal route, and 1 intraoperatively. All of the patients had a history of laparotomy and small bowel resection due to complications such as invagination and ileus. In 7 patients, we found a total of 110 polyps ≥10 mm in diameter (10-100 mm) and polypectomies were performed in all of them. The only complication was a bleeding after polypectomy, which was controlled by sclerotherapy. In 1 patient, because of the intraabdominal adhesions due to past laparotomies, polypectomy was done by intraoperative endoscopy. In 2 of our patients, we made surveillance colonoscopies, found new polyps in the small intestine, and performed polypectomies.* ***Conclusions:*** *Double-balloon endoscopy is an effective and safe endoscopic technique, and represents a milestone for both treatment and surveillance of patients with Peutz-Jeghers syndrome. Polypectomies made in the small intestine might decrease the complication rate due to these polyps and the need for surgery.*

**Key words:** Peutz-Jeghers syndrome, double-balloon endoscopy, polypectomy, surveillance

## Peutz-Jeghers sendromlu hastalarda çift balon endoskopi

***Amaç:*** *Peutz-Jeghers Sendromu, mukokutanöz pigmentasyon ve gastrointestinal sistemde, özellikle ince barsakta hamartomatöz polip varlığı ile karakterize nadir görülen herediter bir hastalıktır. Çift balon endoskopi, ince barsağı görüntülemenin yanı sıra, hastalıklı ince barsak için terapötik yaklaşımlara imkan tanıyan yeni bir endoskopik yöntemdir. Biz bu çalışmada Peutz-Jeghers sendromu hastalarının takip ve tedavisinde çift balon endoskopi kullanımının etkinliğini ve güvenirliğini araştırdık.* ***Yöntem:*** *2007 ve 2010 tarihleri arasında Dokuz Eylül Üniversitesi Tıp Fakültesi Gastroenteroloji Departmanına Peutz-Jeghers sendromu tanısı ile refere edilen 7 hastayı retrospektif olarak inceledik.* ***Bulgular:*** *7 Peutz-Jeghers sendromu hastasına (K/E oranı 2/5) 21'i oral, 9'u anal ve 1 tanesi intraoperatif olmak üzere toplam 31 çift balon endoskopi işlemi yapılmıştır. Hastaların hepsinde daha önce ileus ve invajinasyon gibi nedenlerle laparotomi ve ince barsak rezeksiyon öyküsü bulunmaktadır. 7 hastada ince barsakta toplam 110 adet 1 cm'den büyük polip saptanmış (10–100 mm), hepsine polipektomi yapılmıştır. Sadece 1 hastada polip eksizyonu sırasında skleroterapi gerektiren kanama komplikasyonu izlenmiştir. Bir hastada daha önceki operasyonlara ikincil luminal yapışıklıklar gelişmesi nedeni ile distal ince barsaktaki polipler intraoperatif enteroskopi yapılarak çıkartılmıştır. Hastaların hepsinde ince barsak taraması tamamlanmıştır. İki hastada sürveyans kolonoskopileri yapılmış, hastaların ikisinde de yeni polip gelişimi saptanmış ve tekrar polipektomi yapılmıştır.* ***Sonuç:*** *Çift balon endoskopi, Peutz-Jeghers sendromu tanılı hastaların takip ve tedavisinde dönüm noktası olmuş etkin ve güvenilir bir endoskopik yöntemdir. Çift balon endoskopi ile ince barsaktaki poliplere polipektomi uygulanması, izlemde komplikasyon oranını ve hastaların laparatomi ihtiyaçlarını azaltabilmektedir.*

**Anahtar kelimeler:** Peutz-Jeghers sendromu, çift balon endoskopi, polipektomi, sürveyans

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**Manuscript received:** 09.02.2011 **Accepted:** 23.06.2011

*Turk J Gastroenterol 2012; 23 (5): 496-502*
*doi: 10.4318/tjg.2012.0356*

*Presented as a poster at the 27th National Gastroenterology Congress, 2010, Antalya, Turkey*

## INTRODUCTION

Peutz-Jeghers syndrome (PJS) was first described in 1921 by Peutz (1) and in 1940 by Jeghers (2) as a rare syndrome inherited in an autosomal dominant pattern. It is characterized by hamartomatous polyps of the gastrointestinal tract, mucocutaneous hyperpigmentation and intestinal and extraintestinal tumors (1,2). PJS-related polyps occur most frequently in the small intestine. The incidence of polyps in the small intestine is highest in the jejunum and progressively decreases in the ileum and duodenum. These patients may also have polyps in the colon and stomach, with a frequency of 30% and 25%, respectively. Hamartomatous polyps can also develop outside the gastrointestinal tract, such as in the uterus, nasal cavity, bladder, and lungs (3).

Hyperpigmentation occurs as mucocutaneous macules on the lips, around the mouth, eyes, nostrils, and on the buccal mucosa, and sparsely on the fingers, soles of the feet, palms, anal area, and intestinal mucosa (4). These lesions are caused by pigment-laden macrophages on the dermis. They are evident within the first years of life (often at birth) and increase in size and number over time. Most of the pigmented lesions fade after puberty except for perioral pigmentation, which may persist throughout life. These lesions are flat, blue-grey to brown spots, which are 1-5 mm in size. Malignant degeneration of these lesions is extremely rare (5).

The diagnosis of PJS is defined by the presence of histopathologically confirmed hamartomatous polyps and at least two of the following clinical criteria: family history, hyperpigmentation and polyps in the small bowel (6). There are many different diagnostic tools to detect these polyps in the gastrointestinal tract, such as small bowel series examination, computed tomography (CT), capsule endoscopy, magnetic resonance (MR)/CT enteroclysis, and MR/CT enterography (7). However, double-balloon endoscopy (DBE), which was introduced in clinical practice in 2001, enables both endoscopic visualization of the entire small bowel and therapeutic interventions in a single procedure. The aim of this study was to evaluate the efficacy and safety of DBE for both treatment and surveillance of patients with PJS.

## MATERIALS AND METHODS

In this study, we retrospectively evaluated 7 consecutive patients (Male/Female: 5/2, mean age: 29.1 years, range: 20-41) who were referred to Dokuz Eylul University, Gastroenterology Department, with the diagnosis of PJS between 2007 and 2010. Demographics, size and location of polyps, histological evaluation, and follow-up information were recorded. Epidemiological and clinical characteristics of these 7 patients are presented in Table 1. Among these 7 patients, all had a history of laparotomy and small bowel resection due to complications such as invagination and ileus. All of them had hyperpigmentation as mucocutaneous macules on the lips, around the mouth and on the buccal mucosa (Figure 1). None of our patients had extra-gastrointestinal tumor. Two patients had a family history of the disease.

All DBE procedures were performed by the same endoscopist. DBE was performed by both the anal and oral route for each patient. To confirm the total enteroscopy, we used Indian ink tattooing of the small bowel. No specific preparation was given before oral route, but for the anal approach, bowel cleansing is required as for colonoscopy. Endoscopy was performed under conscious sedation and all patients were monitored for at least two hours at the end of the procedure. Small bowel

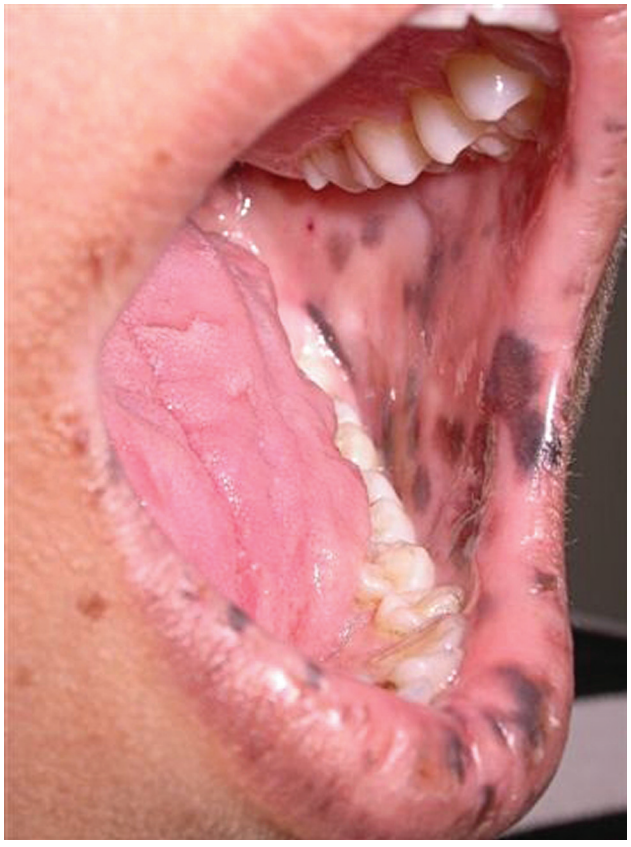

**Figure 1.** Pigmentation of the lips and oral mucosa.

**Table 1.** Patient characteristics and details of DBE procedures

| Number of patients | Number of DBE procedure | Number of polyps removed | Size of the polyps removed | History of abdominal surgery | Complications due to disease | Complications due to DBE procedures | Surveillance |
|---|---|---|---|---|---|---|---|
| 1 | 2 | 2 | 10-20 mm | Right hemicolectomy (2 operations) | Invagination | No | |
| 2 | 2 | 3 | 10-20 mm | Small-bowel excision | Volvulus | No | |
| 3 | 5 | 23 | 10-40 mm | Right hemicolectomy (3 operations) | Ileus, invagination, necrosis of small owel | No | |
| 4 | 6 | 8 | 10-80 mm | Resection of distal ileum and ceacum (2 operations) | Invagination | No | Yes |
| 5 | 6 (1 IODBE) | 30 (six of them were removed intraoperative) | 10-40 mm | Resection of distal jejunum and proximalileum (1 operation) | Ileus | Bleeding and sclerotherapy during polypectomy | Yes |
| 6 | 7 | 26 | 10-100 mm | Small bowel excision (1 operation) | Ileus | No | |
| 7 | 3 | 18 | 10-40 mm | Small bowel excision (4 operations) | Ileus and invagination | No | |

IODBE: Intraoperative double-balloon endoscopy

polyps with a diameter of ≥10 mm were considered to be suitable for polypectomy. We performed polypectomy with a polypectomy snare and removed the excised polyp for histological evaluation. We repeated the DBE procedure until complete removal of all polyps greater than 10 mm, and we scheduled surveillance DBE for two years later. The DBE procedure was repeated earlier if the patient developed symptoms suggestive of small bowel obstruction or due to bleeding. Esophagogastroduodenoscopy and colonoscopy were performed in all patients before DBE, and polyps ≥10 mm in size were also removed endoscopically. Informed consent was obtained from all patients for each procedure. Fujinon EN-450T5 enteroscope was used in all procedures.

### Double-Balloon Endoscopy (DBE) Technique

The DBE system, which was developed by Yamamoto (8), consists of a 200 cm endoscope within a 145 cm overtube. Both the endoscope and overtube have inflatable balloons at their tips, which can be controlled by an air-pump controller. DBE can be performed orally (antegrade approach) or can be introduced into the terminal ileum through the colon (retrograde approach). In the antegrade approach, the endoscope and overtube are both inserted into the stomach with balloons deflated. When the endoscope enters the second portion of the duodenum, the endoscope balloon is inflated. The overtube is advanced along the endoscope. When the distal end of the overtube reaches the end of the endoscope, the balloon of the overtube is also inflated. With both balloons inflated, gentle withdrawal of the overtube causes pleating of the intestine onto the overtube, which prevents looping of the endoscope. Next, the endoscope balloon is deflated and the endoscope is advanced further while the inflated overtube balloon holds the position within the intestine. When the endoscope cannot go any further, the balloon is inflated. The overtube balloon is then deflated and the overtube is advanced to meet the endoscope. By sequential inflating and deflating the balloons in this manner and alternately advancing and withdrawing the endoscope, the small bowel is gathered and shortened over the endoscope allowing for deep insertion of the small bowel (8,9).

## RESULTS

These patients underwent a total of 31 DBE procedures (21 by the oral route and 9 by the anal route and 1 intraoperatively). Complete examination of the small bowel was achieved in all patients. In one patient, because of the intraabdomi-

nal adhesions, polypectomy was performed by intraoperative endoscopy.

In 31 DBE procedures, we found 110 polyps ≥10 mm in diameter (Figure 2a,2b,2c,2d). The number of polyps was highest in the jejunum (n=89) followed by the ileum (n=15) and duodenum (n=6). The maximum size of the polyps was 100 mm in diameter. The only complication was a bleeding after polypectomy, which was controlled by sclerotherapy. The polyps were sent for pathological examination and were found to be hamartomatous polyps characteristic of PJS except for one polyp in the colon having microscopic foci of adenocarcinoma with no stalk invasion. In two of our patients, we made surveillance colonoscopies, found new polyps in the small intestine, and removed them by polypectomies.

## DISCUSSION

Peutz-Jeghers syndrome (PJS) is an inherited autosomal disorder with variable inheritance. The prevalence of PJS is 1 in 8300 to 1 in 280000 individuals (4). It is characterized by hamartomatous polyps in the gastrointestinal tract, mostly in the small bowel and pigmented mucocutaneous lesions. Patients with PJS have a four-fold increased risk of gastrointestinal and non-gastrointestinal cancers compared with general populations. The risk of cancer is highest for gastrointestinal cancers occurring in the esophagus, stomach, small intestine, colon, and pancreas (10). In addition to gastrointestinal cancers, extra-intestinal organs at increased cancer risk include the lung, breast, uterus, cervix, ovaries, and testes.

In PJS, hamartomatous polyps begin growing during the first decade of life, but most patients become symptomatic between the ages of 10 and 30 years. Common presenting symptoms include small bowel intussusception or obstruction (43%) and bleeding or anemia (17%), which cause the patient to undergo repeated operations often involving multiple small bowel resections and anasto-

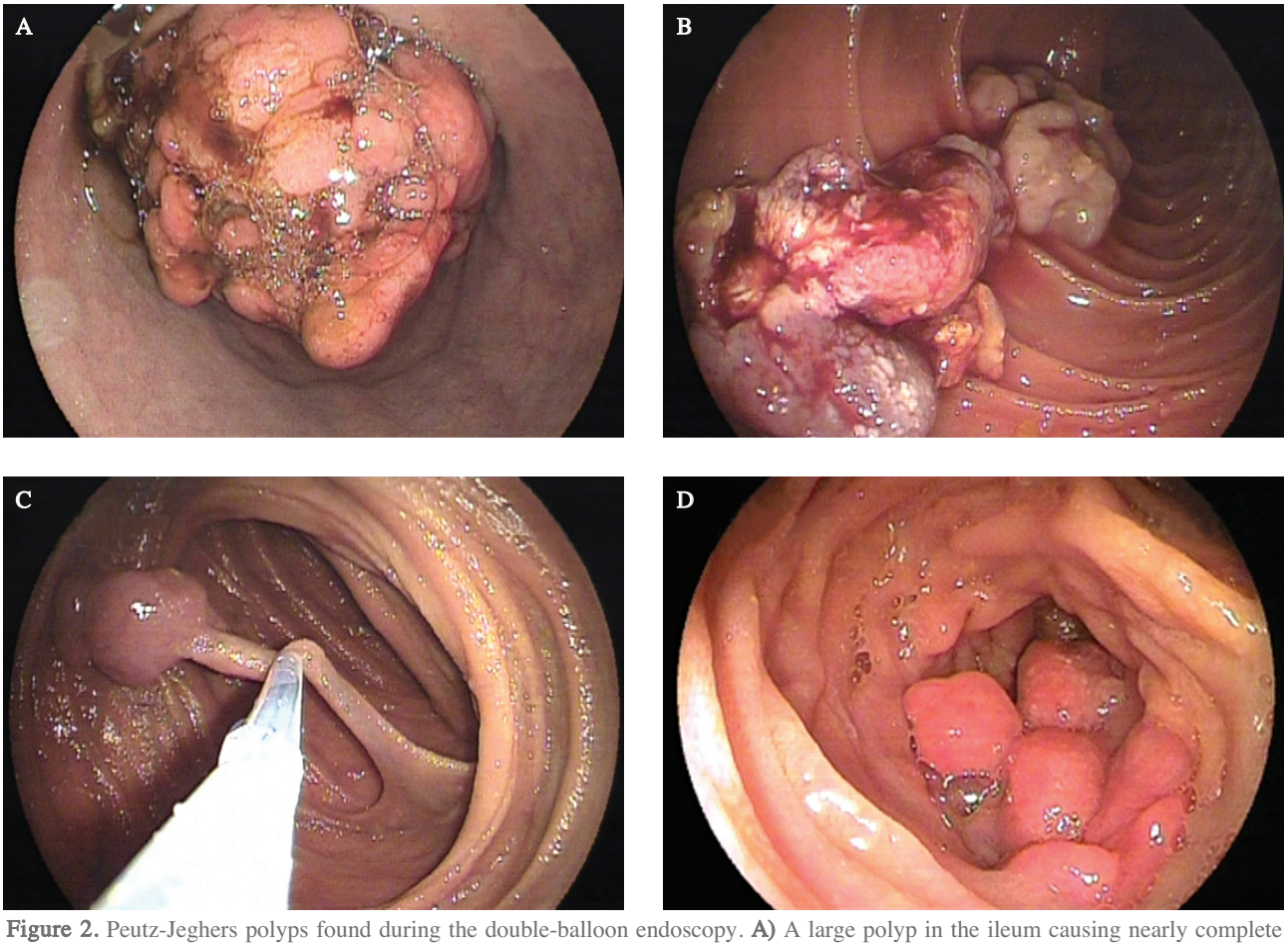


**Figure 2.** Peutz-Jeghers polyps found during the double-balloon endoscopy. **A)** A large polyp in the ileum causing nearly complete obstruction; **B)** Fragments of a large polyp after polypectomy; **C)** Polypectomy of a stalked polyp in the jejunum; and **D)** Numerous Peutz-Jeghers polyps in the jejunum.

moses (11). With the introduction of DBE, the obligation to surgery for management of these life-threatening comorbidities has been decreased. DBE allows the endoscopist to visit areas of the small bowel that were previously unreachable by older techniques. DBE not only enables endoscopic visualization of the small intestine but also tissue sampling and interventional therapies such as polypectomy, so it can be applied for both treatment and surveillance of this disease (12).

In all of our cases, endoscopic examination was performed by DBE and complete examination of the small bowel was achieved in all patients. In one of our patients, we used intraoperative DBE (IODBE) since this is the ultimate method in those patients in whom complete DBE investigation is impossible because of adhesions or other technical complications. It is suitable for those cases in which DBE could not be performed or fails to investigate the entire small intestine, especially to prevent excessive bowel resection (13,14).

Peutz-Jeghers syndrome (PJS)-related polyps occur most frequently in the small intestine. The endoscopic polypectomy procedure performed in the small intestine has some special difficulties. The risk of perforation while working in the small intestine is high due to the thin intestinal wall. Therefore, the endoscopist who performs DBE should be trained not only in endoscopy but also in polypectomy. Another difficulty is removal of the polyps as a whole in order to make histological examination, since these polyps can be very large in size. Getting the enteroscope out of the lumen in order to carry a large polyp outside is very difficult and time-consuming. These polyps can be removed by piece-meal technique. Another solution may be taking biopsies and leaving the resected polyp in the lumen. During DBE, careful attention must be paid not to insufflate too much air in order to avoid intestinal loops, which would impede deep advancement (15). Post-surgical intraabdominal adhesions are another problem that would prevent the free motion of the small intestine within the abdominal cavity, impacting the maximal insertion at DBE. This problem can be solved by IODBE.

The cancer risk in PJS is very high and comes close to that of other high-risk conditions in which surveillance has been recommended. According to a systematic review by van Lier et al. (16), patients with PJS develop malignancies at an average age of 42 years, and the most common malignancy is colorectal cancer. The relative cancer risks varies between 4.8 and 18 compared with the general population, with lifetime cumulative cancer risks up to 93%. On the basis of these elevated risks, there are some surveillance recommendations in order to detect malignancies in an early phase and to remove polyps that may be premalignant and cause complications (16).

In addition to DBE, some other new surveillance techniques are becoming widely available, such as video-capsule endoscopy (VCE) and magnetic resonance imaging (MRI) enteroclysis. It has been shown that VCE and/or MRI are good alternatives to small-bowel follow-through for the detection of small bowel polyps, but they do not provide any opportunity for therapeutic intervention (17,18). DBE is clinically useful and safe for surveillance and also for therapy of polyps in PJS. All patients with PJS have to be monitored lifelong because of the risk of malignancy. It is recommended to start small bowel surveillance at the age of 10, with 2-3-year intervals because of the morbidities caused by hamartomas (16). Benign complications of the polyps, such as bleeding and intussusception, predominate in the first three decades of life, whereas malignancy-related complications become more common thereafter (19). Although the mechanism of carcinogenesis is unknown, a hamartoma-adenoma-carcinoma sequence has been suggested (20). In order to decrease the risk of malignancy, small bowel polyps, which are potentially precursors of cancer, can be removed endoscopically. In our cases, the histological examination of most polyps revealed hamartomatous polyps, with a malignant transformation in one patient. In two of our patients, we performed second-year small bowel polyp surveillance. There were many polyps in both of our patients, which were removed using DBE.

In the literature, there are a limited number of studies about the endoscopic treatment of PJS by DBE (Table 2). Ohmiya (21) reported 18 patients with the diagnosis of PJS and evaluated the usefulness of fluoroscopic enteroclysis (FE), DBE and VCE in polyp detection rates. They concluded that VCE is noninvasive and useful for detection of small bowel polyps in PJS, and DBE is safe and useful for polyp resection without laparotomy. Kopácová (22) compared intraoperative endoscopy and DBE for the diagnosis and treatment of PJS, and stated that polypectomy using DBE may obviate the need for repeated urgent operations and small bowel resections leading to short bowel

**Table 2.** Case series about endoscopic treatment of small bowel polyps by double-balloon endoscopy in patients with Peutz-Jeghers syndrome

| Author | Number of patients | Total number of procedures | Total number of polyps removed | Size of polyps removed | Maximum size of polyps | Complication |
|---|---|---|---|---|---|---|
| 1 Ohmiya N (21) | 18 | 80 | 387 | >5 mm | 50 mm | Perforation (n:1), acute pancreatitis (n:1), post-polypectomy syndrome (n:4) |
| 2 Gao H (7) | 13 | 29 | 79 | >10 mm | 50 mm | No |
| 3 Kopacova M (22) | 10 | 14 | 205 | all polyps | 60 mm | Bleeding after polypectomy (n: 1) |
| 4 Ohmiya N (23) | 2 | 5 | 18 | >10 mm | 60 mm | Fever, abdominal tenderness (n: 1) |
| 5 Plum N (24) | 16 | 47 | 47 | >15 mm | 50 mm | Bleeding (n: 2), perforation (n: 1), propofol associated decrease in oxygen saturation (n: 1) |
| 6 Chen TH (25) | 6 | 12 | NA | >10 mm | 60 mm | No |

syndrome. The other studies are compatible with each other encouraging the use of DBE in PJS.

In conclusion, our experience in patients with PJS indicates that DBE represents a milestone for both the treatment and surveillance of these patients. It offers a useful and safe therapeutic option for small bowel polyps even in patients with a history of abdominal surgery. DBE is not only effective for the treatment of polyps, but also has the potential to prevent future complications like obstruction, intussusception, bleeding, and malignancy, thereby decreasing the need for surgery.

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