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Endoscopic treatment of primary sclerosing cholangitis

Primer sklerozan kolanjitin endoskopik tedavisi

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Background/Aims: *Dominant stricture of an extrahepatic bile duct is responsible for symptoms and an exacerbation of cholestasis in 15-20% of patients with primary sclerosing cholangitis. The aim of this study was to evaluate the efficacy and safety of endoscopic treatment in this selected patient group.* ***Methods:*** *Retrospectively, we evaluated 16 patients who were treated endoscopically due to elevation of serum biochemical liver tests and symptoms which were attributable to dominant bile duct strictures during the period 1990 to 2003. Symptoms and biochemical liver tests were compared before and after treatment.* ***Results:*** *Sixteen patients underwent a total of 58 therapeutic endoscopic retrograde cholangiopancreatographies (ERCP). Sixteen endoscopic sphincterotomies, 15 balloon dilatations, 6 bougie dilatations, 3 stone/sludge extractions and 8 stentings were performed. Endoscopic therapy was technically successful in all patients (100%). Biochemical liver tests were significantly improved when compared with pretreatment values ($p<0.001$). Patients have been followed-up without stents except for the patients who had cholangiocarcinoma and cirrhosis at the beginning. Procedure-related early complications occurred in 8.6% of therapeutic endoscopic biliary procedures. There was no mortality due to endoscopic treatment. Two patients whose stents were changed every two to three months had cholangitis due to stenting during 13 stent periods. Four patients whose stents were changed in seven to 10 days developed suppurative cholangitis (total 6 stent periods).* ***Conclusions:*** *Endoscopic therapy of symptomatic dominant strictures in primary sclerosing cholangitis is safe and effective. The cholangitis seen in long-term stenting seems to be solved by short-term stenting.*

Key words: Primary sclerosing cholangitis, endoscopic treatment

Amaç: *Primer sklerozan kolanjitli hastaların %15-20'sinde ekstrahepatik safra duktuslarının dominant darlığı semptomlara ve kolestazda alevlenmeye yol açabilir. Bu çalışmanın amacı böyle bir hasta grubunda endoskopik tedavinin etkinlik ve güvenliğini tespit etmektir. 1990-2003 yılları arasında dominant safra duktus darlığı nedeniyle endoskopik tedavi yapılan 10 hasta retrospektif olarak değerlendirildi. İşlemden önce ve sonraki semptomlar ve serum biyokimyasal karaciğer testleri karşılaştırıldı.* ***Bulgular:*** *Onaltı hastaya 58 terapötik endoskopik retrograt kolanjiopankreatografi işlemi yapıldı. Onaltı sfinkterotomi, 15 balon dilatasyonu, 6 buji dilatasyonu, 3 taş Içamur ekstraksiyonu ve 8 hastaya stent uygulaması yapıldı. Endoskopik tedavi teknik başarı oranı %100'dü. Klinik bulgularda ve biyokimyasal karaciğer testlerinde belirgin gerileme görüldü. ($p<0.001$). Başlangıçta kolanjiokarsinoma ve sirozu olan hasta dışında hastalar stentsiz izlenmektedir. Erken, işlemle ilgili komplikasyonlar % 8.6 oranında görüldü. Endoskopik tedaviye bağlı herhangi bir mortalite görülmedi. Stenti 2-3 ayda bir değişen hastalarda 13 stent periyodu sırasında 2 hastada kolanjit gelişti. 7-10 günde stenti değişen 4 hastada 6 stent periyodunda süpüratif kolanjit gelişmedi.* ***Sonuç:*** *Primer sklerozan kolanjitte semptomatik dominant striktürlerin endoskopik tedavisi güvenli ve etkilidir. Uzun süreli stentlemede görülen kolanjit probleme kısa süreli stentleme ile çözülmüş gibi görülmektedir.*

Anahtar kelimeler: Primer sklerozan kolanjit, endoskopik tedavi

INTRODUCTION

Primary sclerosing cholangitis (PSC) is a chronic, progressive cholestatic disease with unknown etiology, characterized by fibrosis and inflammation of the biliary tract (1). PSC is frequently associated with inflammatory bowel disease (2).

Multifocal strictures and dilatations of intra and/or extrahepatic bile ducts are the characteristic cholangiographic findings. Strictures deteriorating the clinical situation of patients causing cholangitis, jaundice and abdominal pain, described

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as dominant strictures, are seen in 15-20% of PSC patients (3, 4). An invasive treatment is needed to correct the strictures in this patient group.

Dominant strictures can be treated surgically by stenting, dilatation, resection or bypassing procedures. But a surgical approach has a higher mortality and morbidity rate and also increases the hazards of liver transplantation (5). Since bile ducts are not dilated, the percutaneous technique is difficult and multiple attempts are needed, which increase the risk of the procedure (6). For these reasons, endoscopic treatment modalities have been performed frequently since 1982 for dominant strictures in PSC (7-12).

We aimed to report endoscopic treatment and follow-up results of dominant strictures of 16 PSC patients.

MATERIALS AND METHODS

We reviewed endoscopic treatment results of PSC patients who admitted due to cholangitic symptoms and findings, jaundice, abdominal pain, itching and progression in biochemical cholestatic liver tests during the period 1990 to 2003.

Endoscopic retrograde cholangiopancreatography (ERCP) was performed by TJF duodenoscope (Olympus-Japan). Patients were given antibiotics prophylactically and midazolam and/or meperedine for sedation before procedure. Standard ERCP catheters for cannulation, standard sphnicterotomes with 20-30 mm cutting wire length for endoscopic sphincterotomy (ES), stone extraction balloon for bile duct cleaning and 7 French nasobiliary drains (NBD) for nasobiliary drainage were used. ES was performed in all patients as the easier procedure. Sludge and stones were extracted by extraction balloon. Before stenting, bougie and/or balloon dilatation and/or transient NBD were performed for dominant strictures. Until the last few years, stents were changed every three months or sooner if obstructive symptoms appeared. Stents were extracted in 7 to 10 days in some patients in more recent years. All patients were given ursodeoxycholic acid at a dosage of 15 mg/kg during the follow-up period.

Clinical and laboratory findings showing efficacy of the procedure were compared before and after endoscopic treatment. Short-term and long-term complications related with endoscopic treatments are given.

STATISTICAL ANALYSIS

Mann-Whitney U test was used for comparison of the two groups, and Wilcoxon 2 paired sample test for comparison of variables before and after treatment. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

ERCP was performed on 37 PSC patients and endoscopic treatments were performed on 16 of them (43.2%) over the last 13 years in our clinic. There were 10 men and 6 women (mean age 35±11.2 years), with a follow-up of 28.5±30.4 months (1 month-13 years). Ten patients had inflammatory bowel disease (7 ulcerative colitis, 3 Crohn's disease).

A total of 58 endoscopic procedures (range: 1-19; mean: 3.4) were performed on 16 patients. Eight patients underwent only one ERCP procedure. The main symptoms and findings in patients were as follows: abdominal pain in 27, fatigue in 39, jaundice in 16, icterus in 15, cholangitis in 15, and biochemical cholestasis without symptoms in 2, respectively. Clinical and laboratory findings before and after procedures are given in (Table 1, 2).

Endoscopic sphincterotomy was performed on all patients. A total of 15 balloon dilatations (1-8; mean=2.2) and six bougie dilatations were done. Transient NBD catheters were implanted 15 times (1-7; mean=1.6). Sludge extraction by

Table 1. Clinical findings before and after ERCP

	Before procedure	After procedure
Pain	8	1
Fatigue	15	5
Jaundice	10	1
Itching	11	2
Cholangitis	4	0

*p<0.001

Table 2. Laboratory findings before and after ERCP*

	ALP	GGT	T Bil	D Bil	ALT	AST
Before procedure	1438±1490	359±479	2.4+1.9	1.3±1.5	86±50	86±87
After procedure	735±500	182±172	1.4±1.0	0.5±0.6	44±19	46±18

*For all parameters p<0.001

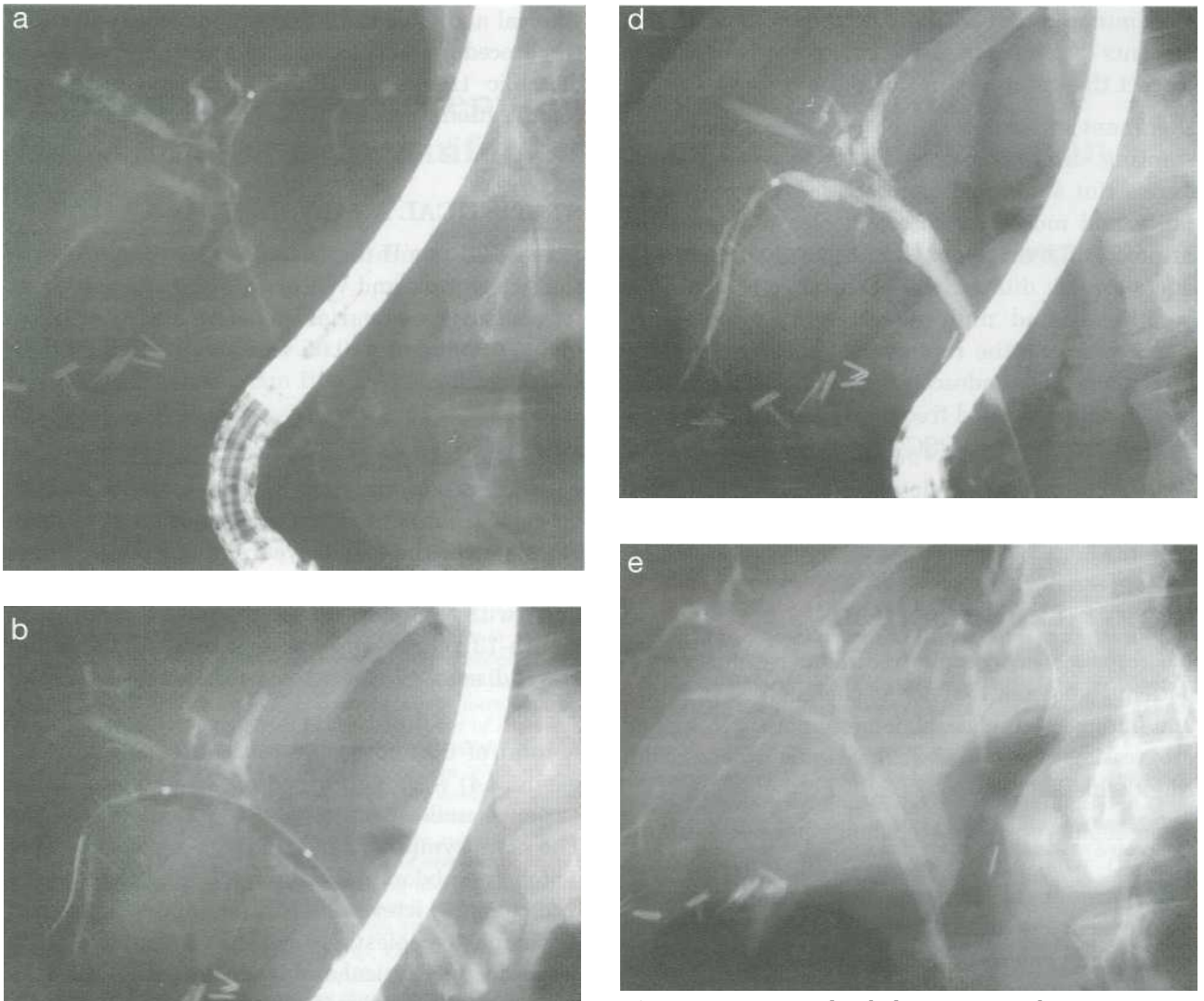

Figure I. Retrograde cholangiograms showing stricture in right and left hepatic duct (a), balloon dilatation of both hepatic ducts (b, c), stenting (d) and significant improvement after stenting (e)

balloons were needed in three patients. Stents were implanted in eight patients. Eight patients were followed by treatments other than stenting. Technical success rate of endoscopic treatments was 100% (Figure la-e).

Eight patients who were followed without stenting had balloon dilatation; two also needed additional bougie dilatation. Five patients had NBD during a one-week period. The patients who had NBD have been followed for approximately 60.5 months (15 months - 6 years) without symptoms. Three patients required no additional endoscopic procedure since sufficient opening was apparently obtained. These patients have been followed up without symptoms for 28.6 (16-65) months.

A total of 29 stents (1-3; mean=1.6) were implanted in eight patients in 19 sessions. Six of these patients have been followed without stenting to date. Four of the six patients have been followed up without stents after one stent period, one after two stent periods, and one after nine stent periods, respectively. Short-term stenting was performed in two patients with one stent period, in one patient at the second of a total of two stent periods, in one patient at the last third of a total of nine stent periods (total 6 stent periods). Others were changed every two or three months (total 13 stent periods). Follow-up period without stents was 32 months (2 months - 4 years). One patient who was followed up with stent had cholangiocellular carcinoma associated with PSC diagnosed during the first ERCP procedure. A metallic stent was implanted in this patient after one plastic stent period. The other patient with stent had secondary biliary cirrhosis with portal hypertension and ascites. This patient had previously undergone a cholecystojejunostomy in a different center.

Clinical and laboratory findings of all patients improved after ERCP procedures (Tables 1-2). Cholangitis especially improved in all patients. Bilirubin, AST, and ALT levels returned to normal or near normal values in all patients except for the patient with cirrhosis. ALP and GGT levels decreased significantly, but did not return to normal values.

Four patients developed cholangitis related to the ERCP procedure. Cholangitis improved in a few days with antibiotic and supportive treatment. One patient required cholecystectomy due to cholecystitis development after procedure. Neither pancreatitis nor bleeding developed in this patient group. Early complication rate was determined as 8.6% (5/58). Two patients developed cholangitis as a long-term complication which improved in a short time with changing of stents, and antibiotic and supportive treatment. The stents of these two patients were changed in the long term period. No patient developed cirrhosis or cholangiocellular carcinoma during follow-up, except for the patients who were diagnosed as cirrhosis and cholangiocellular carcinoma at the beginning. There was no mortality due to endoscopic procedures.

DISCUSSION

Primary sclerosing cholangitis can cause acute clinical detorioration such as bile stasis, bacterial infection or chronic pathologies like destructive cholangitis and secondary biliary cirrhosis. Provision of biliary drainage is especially needed to improve these pathologies in patients with dominant strictures.

Endoscopic treatment was found quite effective for dominant strictures in PSC in this study. There was significant improvent in clinical status and laboratory findings of the patients. We found 16 dominant strictures in 37 PSC patients (43.2%) over the last 13 years in our clinic. This ratio is thought to be higher than the literature (15-20%)(7), most likely attributable to our clinic serving as a referral center for therapeutic ERCP in our country.

The aim of treatment of biliary strictures caused by different etiologies (Table 3) must be known and the method of treatment and efficiency of treatment must be evaluated according to this aim. PSC is different from postoperative biliary strictures if evaluated from this point of view. In contrast to postoperative biliary strictures, the pathology in PSC is progressive. Thus, persistent preservation of the obtained opening is not expected, as it is with postoperative biliary strictures.

Our endoscopic treatment results were similar with those in the literature. Endoscopic success rate was 88% in the study of Lee et al., and 77% of the patients improved clinically, biochemically and radiologically (8). Johnson et al. (9) found a decrease in hospital admission due to cholangitis after endoscopic treatment in 35 PSC patients, van Milligen de Wit and colleagues (10) found significant improvement in laboratory parameters in 84% successful procedures in 25 patients, and 12 patients (57%) were followed up for an average of 29 (2-120) months without stents.

Short-term stenting has been mentioned in literature recently. It was pointed out that it was possible to have persistent response with such an approach. It is mentioned that optimal dilatation time for stents is not known, and that long-term stenting such as two to three months can cause suppurative cholangitis. There are also similar results reported for short-term and long-term stenting. Ponsioen et al. (11) treated the dominant strictures of 32 patients with 7 or 10 French stents for a mean period of 11 days. Complaints of 83% of patients improved significantly. Eighty percent of patients required no additional procedure for one year, and 60% for three years. Seven (15%) complications (perforation, pancreatitis, cholecystitis) were noted in a total of 45 endoscopic procedures,

Table 3. The aim of endoscopic treatment of biliary strictures with different etiologies

Etiology	Aim
Postoperative	Kept without stents
Chronic pancreatitis	Palliation
Portal vein cavernomatous transformation	Palliation
Malignant biliary stenosis	Palliation
Primary sclerosing cholangitis	Correction of dominant trie ture and fo low-up without stent as ong as possible

but none was due to stenting. Suppurative cholangitis risk due to stenting in another series of these authors following changing of the stents every three months was 50% (10). Stent-related cholangitis developed in two of our patients during 13 stent periods in whom stents were changed in two to three months. Five patients of our series who were followed up with 7 F NBD and four patients who were followed up at six short term stenting periods in our series could be viewed as similar with this group.

Kaya et al. (12) compared 34 patients treated with only balloon dilatation to 37 patients treated with stents. They found that stenting resulted in no additional benefit and in fact caused complications. But in the discussion section of this retrospective study, it was pointed out that groups were not randomized. No stents were implanted in the patients who responded to dilatation effectively; stenting was only performed in patients whose dilatation was determined as not sufficient. It was not possible to say dilatation was effective in this situation. Restenosis was also noted in some patients who had been treated only by balloon dilatation (6).

There are no reports in the literature regarding any clinical or endoscopic predictive factors to indicate the response to balloon dilatation or short-term stenting. We had only three patients who were treated solely by balloon dilatation. According to our experience, it could be possible to follow up patients with short segment with no contracted/crumpled strictures during ERCP, without stents.

In conclusion, endoscopic treatment for dominant strictures in PSC is effective and safe. The cholangitis seen in long-term stenting seems to be solved by short-term stenting. Future studies are needed to help determine those patients requiring only dilatation versus short-/long-term stenting.

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