

SAFRA FİSTÜLLERİNDE OCTREOTİDE'NİN TEDAVİ EDİCİ ETKİSİ

THERAPEUTIC EFFECTS OF OCTREOTIDE ON BILIARY FISTULAS

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Özet

Bu klinik çalışmada Octreotide'in safra fistülleri üzerindeki tedavi edici etkisi incelendi. Atatürk üniversitesi Tıp fakültesi Genel Cerrahi A.B.D.'da Mart 1992 ve Aralık 1995 tarihleri arasında tedavi gören 22 hasta çalışmaya dahil edildi. Çalışma grubundaki 12 hastaya standart fistül tedavisi ile birlikte Octreotide, kontrol grubundaki 10 hastaya yalnızca standart fistül tedavisi verildi. Çalışma grubundaki hastaların outputları daha dikkati çeker olmakla birlikte her iki gruptaki hastaların fistül outputları progressif şekilde azaldı (Sırası ile $P < 0.001$, $P < 0.05$). Çalışma grubundaki fistüller en geç 16, kontrol grubundakiler ise en geç 24 günde kapandı. Fistül kapanma zamanları arasındaki fark istatistiksel olarak anlamlı bulundu (Sırayla, 9.0 ± 2.8 gün ve 15.8 ± 6.1 gün, $P < 0.01$). Sonuç olarak Octreotide kullanımının hospitalizasyon süresini ve safra fistülünün kapanma süresini kısaltabileceği ifade edilebilir.

Anahtar kelimeler: *Octreotide, Somatostatin analogu, Safra fistülü, Safra kaçağı*

Summary

This study which investigates the effects of octreotide on biliary fistulas includes 22 patients receiving treatment because of biliary fistulas in Department of General Surgery Atatürk University School of Medicine between March 1992 and December 1995. Twelve patients received octreotide along with standart fistula treatment, whereas the other ten patients only standart fistula treatment. Output of the fistulas was decreased in both groups but more significantly in octreotide group ($P < 0.01$ and $P < 0.05$, respectively). The maximal duration of the fistulas was 16 days in octreotide group, while 24 days in standart treatment group, and the differences between the mean durations were statistically significant (9.0 ± 2.8 days and 15.8 ± 6.1 days respectively, $P < 0, 01$). In conclusion, octreotide may shorten the duration of the fistulas and the hospitalization period.

Key words: *Octreotide, Somatostatin analogue, Biliary fistulas*

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Introduction

External biliary fistulas mainly occur following surgical procedures. Penetrating and blunt traumas also may cause external biliary fistulas (1). Previous studies showed that somatostatin is present in many organisms such as protozoans and fishes (2,3). Octreotide, a synthetic somatostatin analogue, was discovered in 1982 (4,5). Octreotide exerts pharmacologic actions similar to those of native hormone somatostatin (4,6-8). It's clinical use is superior to somatostatin because of its long half-life, and because of its subcutaneous application (9-14). Octreotide has many effects on human body (2,3). It was showed that octreotide decreases exocrine and many endocrine secretions in gastrointestinal tract (4,6,12, 15,16). Some authors have showed the favourable effects of octreotide and somatostatin (8,17), but some authors found no significant effects on biliary fistulas (18). The objective of this study is to research the effects of octreotide on patients with external biliary fistulae.

Patients and Methods

This study includes 22 patients with external biliary fistula but distal biliary obstruction, who were treated in General Surgery Department Atatürk University, School of Medicine between March 1992–December 1995. The absence of distal obstruction was demonstrated by T-tube cholangiography in 10 patients (4 patients in octreotide group and 6 patients in control groups), and peroperatuar cholangiography in 4 patients (2 patients in octreotide group and 2 patients in control groups), and operative findings in the others. Localization of the fistulas was identified by T tube cholangiography in 10, by drains inserted during initial operation in 6 and by clinical findings in the other patients. In 12 patients octreotide (Sandostatin® amp. Sandoz Pharma Ltd. Basel/Switzerland) ($20 \mu\text{g}/\text{kg}/\text{day}$) was administered subcutaneously in addition to standart fistulae treatment (Octreotide group). In the other 10 patients only standart fistulae treatment was administered (Study group).

Table 1. Clinical Findings of Patients in Study Group

Origin of fistula and type of operation	Localization of fistula	Main daily drainage (day / ml)	Closure of fistula(day)
1-Open cholecystectomy + Abscess drainage ⇒ Perforation of gallbladder	Cystic duct	250	5
2-Open cholecystectomy + iatrogenic injury of common bile duct ⇒ Acute cholecystitis	Common bile duct	450	10
3-Whipple procedure⇒ Carcinoma of head of pancreas	Hepaticojejunostomy	750	8
4-Whipple procedure ⇒ Carcinoma of head of pancreas	Hepaticojejunostomy	150	9
5-Open cholecystectomy ⇒ Acute cholecystitis	Cystic duct	400	7
6-Open cholecystectomy ⇒ Cholelithiasis	Cystic duct	1500	9
7-Open cholecystectomy + Exploration of the common bile duct ⇒ Cholelithiasis	Common bile duct	800	6
8-Hepatic trauma	Intrahepatic bile duct	700	10
9-Open cholecystectomy + Exploration of the common bile duct ⇒ Cholelithiasis	Common bile duct	1000	12
10-Open cholecystectomy + Iatrogenic injury of common bile duct ⇒ Acute cholecystitis	Common bile duct	750	16
11-Choledochoduodenostomy⇒Cholelithiasis	Choledochoduodenostomy	600	9
12-Choledochoduodenostomy⇒Cholelithiasis	Choledochoduodenostomy	700	8

In the beginning, two patients in octreotide group were excluded because they refused to continue to receive treatment. The patients were evaluated with the daily fistulae output, and fistulae closing time criteria in addition to standart criteria. Student - t - test was used for statistical analysis.

Results

Drainage of biliary fistulas in octreotide group decreased progressively in follow up period. At the beginning of the treatment the mean output of the fistulas was 671 ± 35 cc/day whereas 107 ± 11 cc/day at the 8 th day of the treatment in study group (t: 0.521, $P < 0.001$). In control group the mean output of the fistulas was 705 ± 18 cc/day at the beginning and 460 ± 22 cc/day at the 8th day (t: 2.67, $P < 0.05$). When compared, these amounts are 671 ± 35 ml/day and 705 ± 18 ml/day respectively at the first day (t: .271, $P > 0.05$) while 107 ± 11 ml/day and 460 ± 22 ml/day respectively within 8 days (t:4.67, $P < 0.001$). Fistulas were closed in 9 ± 2.8 days in octreotide-recvieing group and 15.8 ± 6.1 days in control group (t: 3.37, $P < 0.01$). The longest fistulae closure time was 16 days in octreotide group, while 24 days in control group. Status of the patients of octreotide-recvieing group and control group are shown in Table 1 and Table 2

Discussion

Recently, the use of octreotide has been described in the treatment of a wide variety of gastrointestinal disorders. Several reports have been published

concerning the use of octreotide in different types of fistulas (2,4,6,7,10-13,15). Biliary fistulae is one of the serious complication of the surgical procedures of biliary tract. Because biliary leakage may cause significant early morbidity. Clinically significant bile leakage or biliary fistula occurs in 0.3% to 0.6% of patients who underwent biliary tract surgery (16). Some authors thought that surgical management would be necessary in the treatment of biliary fistulas (19) and others thought that biliary fistulas originated from cystic duct could close spontaneously, so surgical management is necessary only in extrahepatic biliary fistulas (20). Endoscopic sphincterotomy and biliary stent replacement are limited in practice because of the need of technical equipment and experienced personnel (19-21). High mortality rate of the management of biliary fistulas by surgical excision of the fistula tract indicates the need of medical management. On the other hand, the disease has some psychiological and economic effects because the duration of the spontaneous closure is long (20,22). It is known that octreotide, which has been used clinically for 10 years (4,5), supresses bile flow from liver strongly (16,19). Theoretically it must have important effects on spontaneous closure of biliary fistulas. But bile fistula treatment requires good drainage of the fistula and unobstructed bile flow to the intestine. There are some different and opposite ideas in the literature about the relation between octreotide and biliary fistulas. Railo et al (8) have showed the favourable effects of octreotide on spontaneous closure of the fistulas in a clinical study. Similarly Van de Stadt et

Table 2. Clinical Findings of Patients in Control Group

Origin of fistula and type of operation	Localization of fistula	Main daily drainage ml /day	Closure of fistula (day)
1-Open cholecystectomy + iatrogenic injury of common bile duct ⇒ Acute cholecystitis	Common bile duct	400	17
2-Open cholecystectomy+Exploration of the common bile duct ⇒ Acute cholecystitis	Common bile duct	650	11
3-Traumatic common hepatic duct injury⇒ Simple closure and T tube	Common hepatic duct	1000	26
4-Open cholecystectomy+Exploration of the common bile duct ⇒ Cholelithiasis	Common bile duct	750	10
5- Exploration of the common bile duct⇒ Acute cholecystitis+ Acute pancreatitis	Common bile duct	600	13
6-Open cholecystectomy + Exploration of the common bile duct ⇒ Cholelithiasis + Choledocholithiasis	Common bile duct	900	19
7- Open cholecystectomy ⇒ Acute cholecystitis	Cystic duct	600	11
8- Open cholecystectomy ⇒ Acute cholecystitis	Cystic duct	800	8
9-Choledochoduodenostomy⇒Choledocholithiasis	Choledochoduodenostomy	500	19
10-Hepaticojejunostomy	Hepaticojejunostomy	850	24

al (17) reported a positive correlation between octreotide and spontaneous closure of fistulas. On the other hand, Gonzales et al (18) found no significant effects of octreotide on this subject. In our study both octreotide and control groups showed spontaneous closure. But median fistula output was found to be fewer and median closure time was found shorter in octreotide group in our study. In general, irrespective of its effectiveness in promoting fistula closure and healing, octreotide may assist in the management of patients simply by lowering fistula output, thereby limiting fluid and electrolyte losses and allowing easier wound and skin care. These results may support the previous idea about the beneficial effects of octreotide on biliary fistulas. But further clinical studies are needed to research the effects of octreotide on spontaneous closure of biliary fistulas.

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