# PROPHYLACTIC EFFECT OF SOMATOSTATIN ON ERCP-INDUCED PANCREATITIS

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*SUMMARY : The aim of the study was to investigate the effect of somatostatin on ERCP-induced pancreatitis by evaluating serum pancreatic elastase levels of patients. Twenty-four patients undergoing therapeutic ERCP (papillotomy, stent placement, basket appliance) were studied. Patients were divided into 2 groups; Group 1 (12 patients, somatostatin group), group 2 (12 patients, control group). Somatostatin (3.5 μg/kg) was given just before the ERCP by intravenous bolus injection in one minute and after catheterisation of the papilla, 250 μg somatostatin infusion was administered for 4 hours. Serum levels of pancreatic elastase-1 were measured by ELISA just before the exploration and at the 4th and 24th hours after catheterisation of the papilla.*

*Pancreatic elastase-1 levels were above the cut-off point in 2 cases of group 1. Only one of them developed ERCP induced pancreatitis. 4th hour serum elastase levels were above the cut-off point in 5 cases of the control group. Four of them developed pancreatitis but one of them had already pancreatitis just before the exploration. Although number of our cases are limited , somatostatin seems promising in preventing ERCP- induced pancreatitis.*

***Key Words :** Serum Elastase-1, ERCP, Somatostatin.*

## INTRODUCTION

The incidence of ERCP-induced hyperamylasemia is 40-75% and acute pancreatitis is 0.7-7.4 % (5,10). ERCP-induced pancreatitis is a common clinical problem, but its treatment remains nonspesific and primarily supportive. Serum pancreatic elastase-1 level is a good diagnostic immunologic parameter for the diagnosis of early period of acute pancreatitis (8). The suppression of pancreatic exocrine function has long been accepted as a cornerstone in the treatment of acute pancreatitis because pancreatic stimulation in the patient recovering from acute pancreatitis often causes acute exacerbation of the disease. Both somatostatin and its analogue SMS 201-995 suppress pancreatic exocrine and endocrine secretions (3, 20). The aim of this study was to investigate the prophylactic effect of somatostatin on ERCP-induced pancreatitis by measuring serum pancreatic elastase-1.

## MATERIALS AND METHODS

24 patients who underwent ERCP were included in our study and were divided into two equal groups. In the control group, 12 patients (5 female, 7 male, mean age 51.2±8.7 years) received

intravenous (iv) infusion of 250cc isotonic sodium chloride for 4 hours. The somatostatin group (6 female, 6 male, mean age 50.7±5.9 years) received a 3.5 μg/kg iv bolus of somatostatin (Somatostatin UCB, Pharma, Belgium) at the start of ERCP and then, 250 μg iv infusion of somatostatin for 4 hours. All patients gave written informed consent before the study was performed. The inclusion criterium for 24 patients was the canullation of papilla with invasive manipulations (papillotomy, stent implantation, basket appliance etc.). After an overnight fast and premedication consisting of pharyngeal anesthesia with xylocain spray, the patients were sedated with 10 mg midazolam (Dormicum, Roche, Switzerland). Duodenal relaxation was achieved with 40 mg hyoscine-n-butylbromide (Buscopan, Eczacıbaşı,Turkey) iv. An Olympus JF-IT side-viewing duodenoscope was used with an Olympus light source. In all patients, the same contrast medium ( non-ionic Iohexol 300 mg/dl, 672 mOsm/kgH2O) was used. The amount of contrast medium injected into the pancreatic duct was registered in all cases. The endoscopist was blinded to the study groups. Serial blood samples were withdrawn pre-ERCP and at time intervals after ERCP (4th hour, 24th hour) for the measurement of serum levels of pancreatic elastase-1. The levels of serum pancreatic elastase were measured by ELISA with elastase-1 serum test kit (ScheBO. Tech, Medizinisch - Biologische Forschungsgesellschaft GmbH, Wattenberg, Germany). Oral intake was prohibited in all patients for the same period of time. For the statistical serum pancreatic elastase analysis, student t test was used and also, we made the comparison of acute pancreatitis in both groups with Fisher Exact test in SPSS for Windows 6.0, p is significant for 0.05.

## RESULTS

Post-ERCP elevation of serum pancreatic elastase was observed in 2 patients of SMS group at 4 hours and one of these patients was the only one who developed a post-ERCP clinical pancreatitis at 24 hours. On the other hand, the serum pancreatic elastase levels of 5 control patients increased after 4 hours from ERCP and all of them had clinical pancreatitis at 24 hours post-ERCP.

Pancreatic elastase levels were shown in Table-1 for the SMS group and Table-2 for the control group. Also, the type of ERCP manipulations of all cases were shown in these tables too.

There wasn't any statistical difference between the elastase levels of two groups at pre-ERCP (0.88±0.94 and 1.14±1.02) (p=0.51). Also, there weren't any statistical differences between these groups after ERCP at 4 and 24 hours. (p=0.25 and

| | | | Post ERCP | | |
|---|---|---|---|---|---|
| **No** | **Manipulations** | **Pre ERCP** | **4 hours** | **24 hours** | **Acute Pancreatitis** |
| 1 | Oddi sphincter manometry | 0.1 | 4.49 | 4.1 | + |
| 2 | Oddi sphincter manometry | 0.8 | 4.33 | 0.2 | - |
| 3 | Sphincterotomy | 2.7 | 2.8 | 1.1 | - |
| 4 | Sphincterotomy+basket appliance | 0.6 | 0.6 | 0.4 | - |
| 5 | Sphincterotomy | 0.1 | 2.2 | 3.1 | - |
| 6 | Sphincterotomy+stent implantation | 2.5 | 1.4 | 0.5 | - |
| 7 | Sphincterotomy+stent implantation | 0.1 | 0.7 | 0.7 | - |
| 8 | Basket appliance | 0.1 | 0.2 | 0.1 | - |
| 9 | Sphincterotomy | 0.4 | 0.8 | 0.2 | - |
| 10 | Sphincterotomy+basket appliance | 1.7 | 1.1 | 1.1 | - |
| 11 | Oddi sphincter manometry | 1.1 | 1.8 | 0.4 | - |
| 12 | Sphincterotomy | 0.3 | 0.1 | 0.1 | - |

Table 1 : Serum pancreatic elastase levels (ng/mL; cut - off point 3.5 ng/mL), the number of clinical acute pancreatitis, and the kinds of ERCP manipulations of all SMS group cases.

| No | Manipulations | Pre ERCP | Post ERCP 4 hours | Post ERCP 24 hours | Acute Pancreatitis |
|---|---|---|---|---|---|
| 1 | Oddi sphincter manometry | 0.4 | 2.6 | 3.6 | + |
| 2 | Sphincterotomy+basket appliance | 0.6 | 4.8 | 0.5 | + |
| 3 | Sphincterotomy | 0.4 | 0.5 | 0.1 | - |
| 4 | Sphincterotomy+basket appliance | 3.8 | 6.0 | 1.6 | + |
| 5 | Sphincterotomy | 1.5 | 2.5 | 1.1 | - |
| 6 | Sphincterotomy+stent implantation | 0.3 | 1.0 | 1.5 | - |
| 7 | Sphincterotomy | 0.8 | 0.6 | 0.1 | - |
| 8 | Sphincterotomy+stent implantation | 1.1 | 3.2 | 1.0 | - |
| 9 | Oddi sphincter manometry | 2.1 | 3.9 | 2.1 | + |
| 10 | Oddi sphincter manometry | 0.4 | 0.2 | 0.2 | - |
| 11 | Sphincterotomy+basket appliance | 0.6 | 0.1 | 0.1 | - |
| 12 | Sphincterotomy+basket appliance | 1.7 | 6.2 | 3.3 | + |

Table 2 : Serum pancreatic elastase levels (ng/mL; cut - off point 3.5 ng/mL), the number of clinical acute pancreatitis and the kinds of ERCP manupulations of all control group cases.

p=0.60, respectively).

## DISCUSSION

In order to evaluate endoscopic retrograde cholangiopancreatography (ERCP)-induced pancreatitis, we measured serum elastase in 24 patients undergoing ERCP. All of our cases possessed a higher risk of acute clinical pancreatitis compared with the patients who had only diagnostic ERCP without any manipulations to the sphincter. On the other hand, Conn et al. reported that pancreatic duct cannulation was associated with a greater elevation in serum pancreatic enzymes, and papillotomy or stent placement did not influence these changes any further (4).

However, it is the reality that if an additional manipulation is combined with the diagnostic ERCP, the duration can be longer and more contrast medium will be used; so the risk of pancreatitis will also increase. Likewise, acute oedamatous pancreatitis is known as one of the frequent side effects of the Oddi syphincter manometry (14).

The use of somatostatin or its long-acting analogue SMS 201-995 has been reported to reduce the post-ERCP rise in serum amylase levels (2, 3, 6, 11, 17, 23, 24, 25). In the literature, considerable controversy exists about the effect of both somatostatin and SMS 201-995 in preventing enzyme changes and/or pancreatitis after ERCP.

The tetradecapeptide somatostatin has been reported to reduce both basal and secretin-stimulated pancreatic exocrine secretion in man (7, 9, 13, 21). Therefore, it has been used in the treatment of acute pancreatitis (15, 16, 19, 22, 27). On the basis of these findings, it would seem logical to administer somatostatin during and after ERCP in order to reduce the incidence of hyperamylasemia and pancreatitis. Bordos (1) and Guelrub (12) reported that somatostatin infusion during ERCP could prevent pancreatic injury and pancreatitis. Although some studies suggest that somatostatin does not influence hyperamylasemia induced by ERCP (18, 26), it has never been claimed to increase the risk of pancreatitis after ERCP. Our preliminary findings suggest that somatostatin might help to reduce the incidence of ERCP-induced pancreatitis.

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## REFERENCES


1. Bordos JM, Toledo V, Mondelo F, Rodes J : Prevention of pancreatic reactions by bolus somatostatin administration in patients undergoing endoscopic retrograde cholangio-pancreatography and endoscopic sphincterotomy. Hormone Res 1988; 29 : 106-108.
2. Boxter JN, Imrie CW, McKoy CJ : Acute pancreatitis and octreotide. Lancet 1991; 338 : 389.
3. Chol TK, Mok F, Zhon WH, Fon ST, Loi ECS, Won J : Somatostatin in the treatment of acute pancreatitis: a prospective randomized controlled trial. Gut 1989; 30 : 223-227.
4. Conn M, Goldenberg A, Conception L, Mondeli J : The effect of ERCP on circulating pancreatic enzymes and pancreatric protease inhibitors. Am J Gastroenterol 1991; 86 : 1011-1014.
5. Cotton RB : ERCP. Gut 1977; 18 : 316-341.
6. Cotton RB, Lehman G, Vennes J, Geen JE, Russel RCG, Mayers WC, Liguary C, Nickly N : Endoscopic spincterotomy complications and their management: on attempt at consensus. Gastrointest Endosc 1991; 37 : 383-393.
7. Dollinger HC, Raptis S, Pfeiffer EF : Effects of somatostatin on exocrine and endocrine pancreatic function stimulated by intestinal hormones in man. Horm Metab Res 1976; 8 : 74.
8. Dominguez-Munoz J.E, Effert B, Sauerbruch T, Malfertheiner P : Dynamics and factors related with the ERCP - induced elavation of serum pancreatic enzymes. Digestion 1995; 56 A: 280.
9. Domschke S, Domscke W, Rösch W, Konturek SJ, Sprügel W, Mitznegg P, Wünsch E, Demling L : Inhibition by somatostatin of secretin stimulated pancreatic secretion in man. A study with pure pancreatic Juice. Scand J Gastroenterol 1977; 12 : 59.
10. Doppl WE, Weber HP, Temma A, Klör HC, Federlin K : Post ERCP and ES monitoring to detect pancreatic damage. Gastroenterology 1993; 104 : A-7.
11. Editorial : Somatostatin: hormonal and therapeutic roles. Lancet 1985; 2 : 77-78.
12. Guelrud M, Mendoza S, Viera L, Gelrud D : Somatostatin prevent acute pancreatitis after pancreatic duct sphincter hydrostatic balloon dilatation in patients with idiopathic recurrent pancreatitis. Gastrointest Endosc 1992; 36 : 44-47.
13. Hanssen LE, Hanssen KF, Myren J : Inhibition of secretin release and pancreatic bicarbonate secretion by somatostatin infusion in man. Scand J Gastroenterol 1977; 12 : 391.
14. Ryan JP : Motility of the biliary tree. In: Yamada T, editor. Textbook of Gastroenterology Volume I Philadelphia: JB Lippincott company 1991 : 206-210.
15. Ladas SD, Ratis SA : Coservative treatment of acute pancreatitis: the use of somatostatin. Hepato Gastroenterol 1992; 39 : 466 - 469.
16. Limberg B, Kommerel B : Treatment of acute pancreatitis with somatostatin. N Engl J Med 1980; 303 : 284.
17. OiDonnell LJD, Forthing MJG : Therapeutic potential of a long acting somatostatin analogue in gastrointestinal diseases. Gut 1989; 30 : 1165-72.
18. Persson B, Slazch P, Efendic S, Hoggmark A : Can somatostatin prevent injection pancreatitis after ERCP? Hepato - Gastroenterol 1992; 39 : 259-261.
19. Raptis S, Schelegel W, Lehmann E, Dollinger HC, Zoupas CF : Effects of somatostatin exocrine pancreas and the release of duodenal hormones. Metabolism 1978; 27 : 1321.
20. Reicklin S. Somatostatin. N Engl J Med 1983; 309 : 1556-1563.
21. Roncorini L, Vincenzo V, Montanari M, Maurizio M : Effect of somatostatin on exocrine pancreas evaluated on a total external pancreatic fistula of neoplastic origin. Am J Gastroenterol 1983; 78 : 425.
22. Schegel W, Raptis S, Harvey RF, Oliver JM, Pfeiffer EF : Inhibition of cholecystokinin-pancreozymin release by somatostatin. Lancet 1977; 2 : 166.
23. Tomas GY Jr, Tulossay Z, Popp J, Ponsky A, Koronyi L, Kisfoludy S, Kollin E, Steezek K : Effect of somatostatin on the pancreatitis-like biochemical changes due to endoscopic pancreotography. Preliminary Rep Metabolism 1978; 27 (suppl 1) : 1333-1336.
24. Tulossay Z, Papp J, Koronyi L, Slothimeri M, Tomas G : Hormonal and biochemical changes following endoscopic retrograde cholangiopancreotography. Acta Gastroenterol Belg 1981; 3 : 538-44.
25. Tulossay Z, Popp J : The effect of long-acting somatostatin analogue on enzyme changes after endoscopic pancreotography. Gastrointest Endoscopy 1991; 37 : 48-50.
26. Tydon G, Nyberg B, Sonnenfold T, Thulin L : Effect of somatostatin hyperamylasemia following endoscopic pancreotography. Acta Chir Scand 1986; 530 : 43-45.
27. Usadel K, Leuschner U, Uberla K : Treatment of acute pancreatitis with somatostatin: A multicenter double blind trial. N Eng J Med 1980; 303 : 999.