



## Original Article

# Opium Effects on Pancreatobiliary System in Opium Abusers Evaluated by Endoscopic Ultrasonography

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**Background:** Opium use is a significant social and public health issue. There are numerous effects of opium documented as affecting the pancreatobiliary system. The aim of the study was to assess the pancreatobiliary changes in patients with opium addiction by endoscopic ultrasonography (EUS).

**Methods:** During the study period, consecutive patients who were referred for EUS of submucosal upper gastrointestinal lesions were included. The history of opium addiction and clinical symptoms were recorded prospectively. Diameters of the common bile duct (CBD), pancreatic duct (PD), size of the ampulla of Vater, and gallbladder abnormalities were evaluated using EUS.

**Results:** A total of 254 patients (53.1% male, mean age of 55.4±14.2 years) were studied. A history of opium addiction was present in 56 patients (22.0%). Choledocholithiasis was found in two patients (3.6%) and one control (0.5%) patient ( $P=0.06$ ). Gallbladder stones were found in 13 opium-addict (23.2%) and 16 control (8.1%) patients ( $P=0.002$ ). The mean diameter of the CBD, size of the ampulla of Vater ( $P<0.001$ ), and PD ( $P=0.04$ ) were all significantly greater in patients with opium addiction.

**Conclusion:** Dilation of the biliary and PDs is seen more commonly in patients addicted to opium. However, the clinical implications of these findings need to be further evaluated in future studies.

**Keywords:** Opium, Endosonography, Biliary tract, Pancreatic duct, Sphincter of Oddi dysfunction

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**Received:** December 2, 2022, **Accepted:** July 20, 2023, **ePublished:** October 30, 2023**Introduction**

Opium has several effects on the gastrointestinal tract. One of the most widely recognized aspects of the prolonged use of opium is its effects on the pancreatobiliary system. First and foremost, opium can cause biliary dilation. The mechanism responsible for this finding can be due to an increase in both basic pressure and frequency of phasic contractions of the sphincter of Oddi (SOD), leading to an increase in intraluminal pressure of the common bile duct (CBD).<sup>1-3</sup> These patients usually present with biliary pain as well as dilated bile ducts, even though asymptomatic bile duct dilation has been described in patients with opium addiction, too.<sup>4,5</sup>

The etiology of CBD dilation may be found via transabdominal ultrasonography (TUS) for cases in which the CBD enlargement is due to mechanical obstruction. The cause of extrahepatic bile duct dilation might be a CBD stone or periampullary lesions, including tumors of the distal CBD, pancreatic head, ampulla of Vater, and the second portion of the duodenum. Although TUS can detect large CBD stones and sometimes large pancreatic masses, it provides only modest diagnostic accuracy in diagnosing distal CBD stones and periampullary lesions because of overlying bowel gas. In addition, ultrasound quality is extremely operator-dependent.<sup>6,7</sup>

Although endoscopic ultrasonography (EUS) is operator-dependent as well, it is one of the best imaging modalities for evaluations of both the periampullary area and the diameters and wall thicknesses of biliary and pancreatic ducts (PDs). Furthermore, bowel gas does not affect its accuracy. In this study, we aimed to evaluate pancreatobiliary abnormalities found on EUS in opium-addict patients.

**Materials and Methods**

In the current cross-sectional study conducted from January 2018 to June 2019, 254 consecutive adult patients were referred to our center for EUS and evaluation of sub-epithelial lesions in the upper gastrointestinal tract and were included in the study. Exclusion criteria were age younger than 20, anatomical alterations due to previous surgeries in the upper gastrointestinal tract, obstructive pancreatobiliary disorders, and lack of informed consent.

Cases were defined as patients questioned admitting to abusing opium (either in the past or currently). The control group was comprised of patients for whom no opium use was detected.

Patients were examined after an overnight fast with the patient in the left lateral decubitus position under deep sedation with propofol given by an anesthesiologist.



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EUS was performed using a linear echoendoscope (EG-3870UTK, Pentax Optical Co Ltd, Tokyo-Japan) having a frequency of 5 MHz. The periampullary area was examined as were proximal and distal CBD diameters, CBD and gall bladder (GB) wall thicknesses, ampullary dimensions, PD diameters in the head and body portions of the pancreas, the presence of gallstones or biliary sludge, and other abnormalities including causes of CBD or PD dilation. A CBD was considered dilated when measured at greater than 6 mm in patients with an intact GB or more than 9 mm in patients with a previous cholecystectomy. PD dilation was defined as a PD diameter greater than 3 and 2 mm in the head and body of the pancreas, respectively.

GB and CBD were considered thickened if wall thicknesses exceeded 3 and 1.5 mm, respectively. The size of the ampulla of Vater was measured based on the formula used in a study by Skalicky et al<sup>8</sup>:

$$\text{Ampulla size} = \frac{\text{ampulla width} \times \text{ampulla length}}{2.54}$$

Finally, the portal vein diameter was also measured.

We estimated that a sample size of 54 patients in each group would be required to show a significant difference for an alpha error of 0.05, and a statistical power of 0.8, assuming a standard deviation of 2.58 cm for a mean difference of 1.41 cm between two groups.

## Results

During the study period, 254 patients (53% male with a mean age of  $55.4 \pm 14.2$ ) were referred for EUS for evaluation of sub-epithelial lesions in the upper gastrointestinal tract. A history of opium addiction was noted in 56 patients (22%). The route of opium use was through inhalation in 37 patients (66.1%) and orally in 19 (33.9%) patients. 28 patients had undergone a previous cholecystectomy (7 patients, 12.5% in cases versus 21 patients, 10.6% in the control group,  $P=0.69$ ). Table 1 illustrates the patients' presenting symptoms. No significant differences were noted regarding clinical manifestations, including abdominal pain, nausea, and vomiting, when comparing both groups. Seven (12.5%) opium-addicted patients and 35 (17.7%) controls provided a history of abdominal pain ( $P=0.36$ ).

Gallbladder stones were diagnosed in 13 cases and 16 controls (23.2% vs 8.1%,  $P=0.002$ ). Moreover,

**Table 1.** Clinical manifestation in candidates for endoscopic ultrasound

Clinical manifestation	Number	Percent
Nausea, vomiting	15	5.9
Anorexia	3	1.2
Weight loss	9	3.5
Abdominal pain	42	16.5
Constipation	2	0.8
Fever and chills	1	0.4
Pruritus	1	0.4

choledocholithiasis was detected in two opium-addicted patients and one patient in the control group ( $P=0.61$ ); the bile duct was dilated in all three of these patients. Juxta-ampullary diverticula were noted in two cases compared with none in the controls ( $P=0.008$ ). We found no peri-ampullary tumors in any of the patients.

Table 2 illustrates the measurements of the pancreatobiliary system. All mean diameter parameters were significantly different between the two groups. The mean portal vein diameter was greater in patients with a history of opium addiction. We did not find any evidence of liver disease in any of the patients.

## Discussion

A few studies have reported pancreatobiliary changes amongst opium addicts. The current study demonstrates that in addition to larger diameters in both the main bile and PDs, the rates of GB, as well as biliary duct abnormalities, are greater in patients with opium addiction compared to controls.

A study of 12 767 autopsies by Hwang reported a total GB stone incidence of 6.6%.<sup>9</sup> That study included 43 patients with opium addiction, and 18 (41.9%) of these exhibited GB stones. Sharma et al reported EUS findings in 15 patients with opium addiction who presented with abdominal pain.<sup>10</sup> None of those patients had GB stones. This discrepant finding might be due, at least in part, to the small number of patients in their sample. The frequency of GB stones in our population with opium addiction was greater than in the controls (23.2% vs 8.1%). Moreover, although the frequency of CBD stones was not significantly different, there was a trend towards a greater frequency of CBD stones in the patients with opium addiction ( $P=0.06$ ). Thus, further studies with larger sample sizes are needed to more confidently confirm this finding.

**Table 2.** Pancreatobiliary measurements in patients with opium addiction (OA) and control (C) patients

Variable	Group	Mean (mm)	SD	P value
GB wall thickness	OA	2.6	0.8	0.023
	C	2.4	0.7	
Mid-CBD diameter	OA	7.3	2.8	<0001
	C	4.5	1.5	
Distal CBD diameter	OA	4.2	1.7	<0.001
	C	3.0	1.0	
PD diameter (head)	OA	3.3	1.2	<0.001
	C	2.2	0.7	
PD diameter (body)	OA	1.8	0.6	0.042
	C	1.6	0.6	
Ampulla of Vater surface area	OA	39.1	19.0	<0.001
	C	28.2	13.5	
Portal vein diameter	OA	10.5	2.1	<0.001
	C	8.9	2.1	

Abbreviations: GB, gallbladder; CBD, common bile duct; PD, pancreatic duct.

**Table 3.** Biliary findings in patients with opium addiction in different studies

Author	Year of study	Study design	Country	Imaging	Sample size (addicts/control)	Main finding
Chuah et al <sup>5</sup>	2003	Case-Control	Singapore	TUS	7 / 7	Dilated CBD in OA
Farahmand et al <sup>4</sup>	2007	Cross-sectional	Iran	TUS	110 / 0	Dilated CBD in 65.5% of OA
Zahedi-Nejad et al <sup>11</sup>	2010	Case-Control	Iran	TUS	121 / 142	Dilated CBD in OA
Sharma et al <sup>10</sup>	2013	Case series	India	EUS	15 / 0	Dilated CBD in OA
Dadpour et al <sup>12</sup>	2016	Cross-sectional	Iran	TUS, ERCP	50 / 0	Dilated CBD in OA

Abbreviations: TUS, transabdominal ultrasonography; EUS, endoscopic ultrasonography; ERCP, endoscopic retrograde cholangiopancreatography; CBD, common bile duct; OA, opium addict.

In Table 3 we summarize the pancreatobiliary abnormalities as reported in different study populations. In nearly all of the studies, the mean CBD diameter was increased amongst opium addicts compared with control groups.

To the best of our knowledge, this study is the largest one, having used EUS to compare abnormalities of the pancreatobiliary system in both patients with opium addiction and controls. These biliary changes include abnormalities in distal CBD wall thickness, ampulla of Vater diameter, and the PD diameters as measured in different parts of the pancreas - variables that cannot be properly evaluated with TUS.

We have shown that in comparison with control patients, patients with opium addiction exhibit larger ampulla of Vater, a finding compatible with that reported by Sharma et al.<sup>10</sup> However, the size of the ampulla of Vater in Sharma and colleagues' study was greater than that reported in our study (71.9 vs 39.1 mm<sup>2</sup>). This difference might, at least in part, be due to the longer duration of opium addiction in their patient population. What is of great clinical relevance is that this enlarged ampullary size could be considered attributable to ampullary neoplasms as part of an important differential diagnosis. In these instances, EUS, especially when accompanied by fine needle aspiration/biopsy (FNAB), is a very helpful minimally invasive procedure for differentiating benign from malignant lesions. Moreover, it is possible at EUS to look for regional lymphadenopathy as well as perform FNAB for such findings when present - a procedure that cannot be as readily carried out when using other imaging modalities.<sup>13</sup>

Although in Sharma and colleagues' study,<sup>10</sup> CBD dilatation was noted in all 15 cases, PD dilation in the pancreatic body was detected in only two cases. In contradistinction, amongst our 56 cases, all patients exhibited both dilated CBDs and PDs. The mechanism of PD dilation in these cases might be due to SOD with or without pancreatic sphincter dysfunction. Dilation of both the CBD and PD also can mimic periampullary tumors and might require more investigation, including EUS-guided FNAB and side-view endoscopy for a complete investigation of the ampulla, taking endoscopic biopsies if needed. The portal vein diameter was significantly greater in patients with opium addiction when compared with controls. We do not have any explanation for this

finding that has not been reported before and requires confirmation.

### Conclusion

In conclusion, dilation of both CBD and PD in patients with opium addiction is more prevalent than in control patients. As a result, opium addiction should be considered as a benign cause of dilated pancreatobiliary ducts as well as of enlarged ampulla. Recognition of such differences is clinically pertinent, and long-term follow-up studies are required to better characterize the clinical importance of these findings.

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### Authors' Contribution

All authors participated in the study design and conception. Rasoul Sotoudehmanesh and Mohammad Bagheri performed EUS. Roya Rahimi collected the data; Ali Ali Asgari analysed the data. Rasoul Sotoudehmanesh wrote the first draft of the manuscript and all authors revised it critically.

### Competing Interests

The authors declare no conflict of interest related to this work.

### Ethical Approval

The study protocol was approved by the ethics committee of the Digestive Diseases Research Institute (DDRI) of the Tehran University of Medical Sciences (No. IRB28842-37-01-94).

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