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Common Bile Duct (CBD) diameter in opium-addicted men: Comparison with non-addict controls

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Summary

Background:	Opium and its derivatives are widely abused throughout the world. Recent case reports and a few limited studies have suggested that opiates cause dilation of the common bile duct of the abusers.
Material/Methods:	Our case-control study, lasting 7.5 months, investigated 121 male adult addicts and 142 non-addicted controls for biliary tract diameters, using ultrasonography. The study was conducted in Bahonar Hospital in Kerman. Neither the addiction cases nor the non-addict controls revealed any hepatobiliary tract symptoms. The subjects were asked to fill in a questionnaire. After the exclusion of the symptomatic cases, ultrasound examinations were carried out and the findings from questionnaires and US examinations were recorded.
Results:	The mean \pm SD diameter of the common bile duct was 4.78 ± 2.58 for addicts and 3.37 ± 2.25 for non-addicts. CBD wall thickness was 1.969 ± 0.61 mm in addicts versus 1.73 ± 0.631 in non-addicts. The differences were statistically significant. According to the multivariate analysis, the duration of opium abuse was a significant factor.
Conclusions:	We concluded that CBD dilation and increased CBD wall thickness can be expected in people with a prolonged history of opiate addiction.
Key words:	opium • addiction • CBD • common bile duct • Kerman • Iran
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Background

Opium, being a juice extracted from opium poppy and solidifying into a brownish material originally used for medical purposes, reveals strong habit-forming properties and is abused by many people in most countries, including Iran. Addiction is considered to be a mental disorder which requires medical intervention [1] but it should be remembered that it affects all aspects of the victim's life. Opiate dependence results in many social problems of the victim, his family and community. Furthermore, it carries many health hazards for the abusers, which has been discussed for many years now [2].

Opiates affect the physiological function of the Oddi's sphincter which delays gallbladder emptying [3–6].

Scattered case reports mention the possibility of either common bile duct (CBD) dilation [7–10] or constriction [11].

A recent publication from Singapore reported a more dilated CBD in seven addicts with GI symptoms than in seven non-addicts [7]. Next, there was a report by Rafsanjan from Iran, evaluating a group of 100 opiate addicts and supporting the aforementioned observations [12]. However, the report did not have a control group to compare with. Furthermore, the reason for such a dilation is not clear. Should it be just a mechanical effect of the Oddi's sphincter dysfunction? Is it possible that some inflammatory changes in the hepatobiliary system are involved? CBD wall thickness can provide indirect information regarding the second question.

The purpose of this study was to measure and to compare the common bile duct diameter and CBD wall thickness in a group of opium addicts and in an age-matched non-addict control group composed of people living in Kerman, Iran.

Material and Methods

Ethical Committee of the Kerman University of Medical Sciences had approved the proposals and the study protocol.

During an eight-month period, from July 2008 to March 2009, all male patients 'with non- hepatobiliary problems' referred to the Martyr Bahonar Medical Center of Kerman for ultra-sound (US) evaluation were asked to take part in the study. If their response was positive, a written consent was obtained and an abdominal US was performed, which included measurement of the liver span, spleen, portal vein, and CBD diameters as well as CBD wall thickness. The same radiologist performed all US tests.

After completion of the imaging examinations, a nurse filled in a questionnaire regarding the addiction status, demographic parameters and exclusion criteria, questioning the patient and/or his/her family members in a face-to-face manner.

To increase the sample size, all asymptomatic family members of the participants were also invited to take part in the study.

In order to blind the study, the radiologist was not informed on the patient's addiction status – imaging studies and measurements were performed before questioning the patient, so the radiologist was unaware of the subject's addiction behavior.

Inclusion criteria for the study group of addicts were as follows:

- Age of 20 years or more.
- Confirmed opium addiction for at least 1 year or more.
- Regular opium use – at least twice a week.
- Absence of any of the exclusion criteria.

Inclusion criteria for the control group were the same, except for the addiction, which had to be inexistent.

Exclusion criteria for both groups were as follows:

- Heroin users or abusers of more potent opiate derivatives were excluded because of a more complex nature of their addiction.
- Any symptoms of potential hepatobiliary disorders.
- Any history of jaundice and/or hepatitis.
- Any history of gallbladder illnesses.
- Any kind of proved hemolytic anemia.
- Any history of upper abdominal surgery and/or laparoscopy.
- Any history of significant congenital anomalies.
- History of frequent analgesic, sedative or anticholinergic drug consumption.

After submission of a written consent, all patients underwent abdominal sonography by means of a Sonoline Siemna: Siemens GM-6600A2E200 sonomachine and Probe 3.5–5 Mega HZ. L40. All ultrasonographic studies were performed by the same radiologist. The procedure included: visualization of extrahepatic bile ducts and measurements of common bile duct caliber at its widest point. CBD wall

thickness, portal vein diameter, liver span at the midclavicular line, and spleen span in a window allowing for hilum visualization were also measured as extra parameters.

The subjects were examined in the supine position, following a deep inspiration. At first, we measured the liver span in the parasagittal plane in the midclavicular line. This was followed by the measurements of the inner diameter of CBD and portal vein. To measure the CBD caliber we used the right anterior subcostal window in the longitudinal view and recorded the caliber at its widest point.

After completion of the sonographic examination, a trained nurse administered a questionnaire containing questions on: demographic and addiction behaviors, history of past or current illnesses. Exclusion criteria were applied at this point.

All data were collected in a database using SPSS ver.16.

The data were analyzed with the use of the same software. Demographic data were included in the frequency tables, and mean values of measurements were compared using independent sample t-tests. P values of less than 0.05 were considered as statistically significant. Since in primary evaluations it seemed that the age of subjects and duration of addiction are important predictors, a multivariate analysis was performed in which CBD diameter and wall thickness were considered as dependent variables, while age, addiction, duration of addiction, and daily opium dose, as independent variables.

Results

A total of 343 subjects were originally invited to take part in the study. Forty-nine of them did not agree with the protocol, 9 patients had a history of upper abdominal surgery, 3 subjects were heroin abusers and 19 individuals were intermittent opium users. All of them were excluded from the study. The remaining 263 subject, including 121 opium addicts and 142 non-addict controls, remained for the analysis.

Chief complaints (and the most frequent ones) were nearly the same in both groups, i.e.: asthma, COPD, and car accidents.

The common bile duct diameter showed a significant positive correlation with the duration of opium addiction; the mean diameter of CBD was significantly higher in addicts than in non-addicts and the mean wall thicknesses value was significantly different in two groups.

The habit of smoking cigarettes was significantly correlated with the addiction.

Multivariate analysis confirmed the associations found in the independent sample t-test. However, the latter test showed that both the age of the subjects and the duration of opium abuse have a strong correlation with CBD caliber and CBD wall thickness. Interestingly, the caliber of the CBD increases with increasing duration of the addiction (but only to the maximum of about 20 years, after which the CBD caliber gradually declines).

Table 1. Demographic characteristics of the two groups.

	Addiction	N	Mean	Std. deviation	Std. error of the mean	Statistical significance
Age	Yes	121	42.07	11.564	1.051	.746
	No	142	42.64	15.784	1.325	
Height	Yes	121	169.529	8.2765	.7524	.631
	No	142	170.032	8.5839	.7203	
Weight	Yes	121	67.256	12.8806	1.1710	.000
	No	142	72.761	12.0070	1.0076	

Table 2. A comparison of ultrasound findings between two groups.

	Addiction	N	Mean	Std. deviation	Std. error of the mean	Statistical significance
Liver Span	Yes	121	108.515	16.4992	1.4999	.000
	No	142	127.054	15.4491	1.2965	
Spleen Span	Yes	121	93.208	16.2909	1.4810	.321
	No	142	95.082	14.2568	1.1964	
Portal Vein Diameter	Yes	121	10.410	1.5935	.1449	.694
	No	142	10.336	1.4568	.1222	
Common Bile Duct	Yes	121	4.780	2.5827	.2348	.000
	No	142	3.370	2.2500	.1888	
CBD Wall Thickness	Yes	121	1.969	.6099	.0554	.002
	No	142	1.732	.6309	.0529	

Demographic parameters of the study subjects and controls were summarized in Table 1.

Table 2 included ultrasonographic findings of the two groups and compared them.

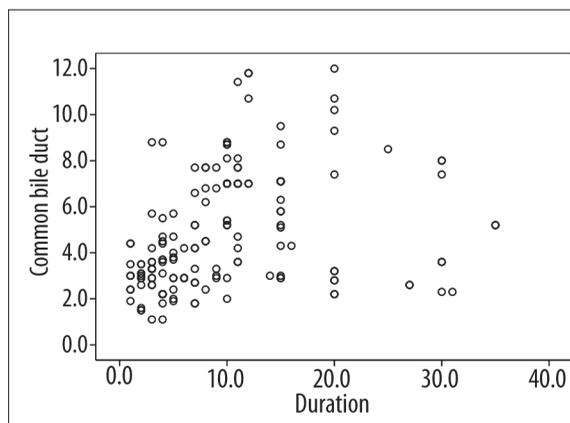
Figure 1 – demonstrated the correlation between CBD caliber and duration of addiction.

Discussion

Imaging textbooks have been presenting various values of the common bile duct caliber, depending on the method of measurement. Lower values were obtained in ultrasound imaging [13,14] while the higher ones in computed tomography scanning (CT-Scan) [15]. The values obtained by us were closer to the reported ultrasonic measurements.

According to our knowledge, this is the first case-control study comparing biliary tract ultrasonographic results of opium addicts with the ones of non-addicts.

At first glance, our results support previous reports regarding the dilating effects of opiates on the common bile duct. However, we found that this is the duration of opium abuse and not merely the presence of addiction which reveals the

**Figure 1.** Common bile duct caliber changes with increasing duration of addiction.

highest correlation with CBD. The answer to the question "Are you addicted to opium" did not directly correlate with CBD caliber because the history of opium abuse was too short in our population and thus CBD had not enough time to become dilated in response to opium. Many reports concern very young populations living in Iran [16,17]. We hope that in the nearest future, studies will be including older populations as well.

Table 3. Significance of various variables in determination Common bile duct diameter and it's wall thickness as revealed by multivariate analysis.

Dependent variable Addiction = yes	Parameter	Beta	St. error	t	Sig	95% confidence interval	
						Lower bound	Upper bound
CBD	Intercept	3.650	.747	4.88	.00	2.17	5.13
	Amount	-.293	.587	-.50	.62	-1.454	.867
	Age	.008	.019	.412	.681	-.029	.044
	Duration	.097	.033	2.95	.004	.032	.161
CBD wall thickness	Dintercept	1.532	.192	7.99	.00	1.153	1.911
	Amount	-.13	.151	-.86	.39	-.427	.168
	Age	.009	.005	1.96	.052	-.0008	.019
	Duration	.011	.008	1.32	.19	-.005	.011

We should also pay attention to an independent CBD-dilating factor of the aging process [15], which has been related to fragmentation of longitudinal smooth muscle bundles and of the intervening connective tissue of the CBD wall [15]. This finding can imply that some of the CBD enlargements observed in chronic opiate abusers may be due to aging, which in combination with pharmacological effects of opiates impairs the structure of longitudinal smooth muscles of the CBD wall.

The overall diameters of CBD measured by means of computed tomography (CT) and reported in the previously mentioned study were higher than in our series; this finding seems related to either different measuring methods (US versus CT scanning) or racial differences.

Another result of our study was the significantly increased thickness of the CBD wall in the addict group. Its connection with potential inflammatory effects of opiate metabolites on the bile of the addicts will be a subject of future studies. Furthermore, liver span in addicts was smaller than in the controls and the difference was statistically significant. We have no explanation for that.

An interesting result of our study was the one connected with the CBD caliber increasing in the addict group for as

long as 20 years of addiction and decreasing afterwards, together with the number of cases. This finding is most probably related to young age of our population. Another explanation can be the 'recall bias' of patients regarding the duration of their addiction. However, considering the fact that serious underlying pathologies had been previously reported in asymptomatic addicts with CBD dilation, the finding can also imply that older patients with dilated CBDs succumbed to hidden underlying conditions and did not survive to continue their habit. Nevertheless, this interpretation was not documented in our study and needs further investigations in opium addicts.

The CBD wall thickness in the group of addicts was also significantly higher than in the control group. This finding requires further studies to rule out a possible inflammation in the hepatobiliary system of opium addicts.

Conclusions

We conclude that CBD dilation can be expected in people with a prolonged history of opiate addiction. However, an enlarged CBD cannot be interpreted as normal (neither in addicts nor in non-addicted elderly subjects) and further evaluation of potential underlying pathologies should be undertaken in such cases.

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