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High drain amylase and lipase values predict post-operative pancreatitis for choledochal cyst

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ABSTRACT

Background: Post-operative pancreatitis is a severe complication after cyst excision with hepaticoenterostomy (CEHE) for choledochal cysts. The aim of this study was to examine the dynamic post-operative changes in drain amylase and lipase values after CEHE for choledochal cysts, and then compare these values with the clinical outcomes in order to identify risk factors for post-operative pancreatitis after CEHE. **Patients and Methods:** A total of 19 patients with choledochal cysts were retrospectively examined in the period between 2005 and 2012. The amylase and lipase values in the drainage and the serum, and the output of the effluent were measured post-operatively. The associations between their values and the clinical outcomes were evaluated. **Results:** Six were found to have a pancreatic leak according to an international study group definition. In two of them, who developed post-operative pancreatitis, both amylase and lipase values in drainage were markedly elevated at 1 post-operative day (1 POD). The drain amylase value seemed to elevate rather specifically dependent on the occurrence of post-operative pancreatitis, whereas the drain lipase value tended to elevate regardless of the presence/absence of post-operative pancreatitis. **Conclusion:** It was indicated that amylase and lipase values in drainage at 1 POD could be effective predictors of post-operative pancreatitis after CEHE.

Key words: Child, choledochal cyst, drain amylase, drain lipase, post-operative pancreatitis

INTRODUCTION

Post-operative pancreatitis after cyst excision with hepaticoenterostomy (CEHE) for choledochal cysts is rare (4-5%); however, when it occurs, invasive management such as surgical or endoscopic procedures is often required.[1,2] High levels of amylase in ascites were identified in both acute and chronic pancreatitis in children.[3,4] Closed abdominal drainage was performed post-operatively in patients with CEHE, and we hypothesized that the drain amylase and lipase values could be used to predict post-operative pancreatitis after CEHE. The aim of this study was to examine the dynamic post-operative changes in drain amylase and lipase values after CEHE for choledochal cysts, and then compare these values with the clinical outcomes in order to identify risk factors for post-operative pancreatitis after CEHE. Here, we describe our experience of 19 patients undergoing CEHE for choledochal cysts, whose amylase and lipase values in drainage were measured post-operatively, indicating the usefulness of analysing the amylase and lipase values in drainage to predict post-operative pancreatitis.

PATIENTS AND METHODS

A retrospective chart review was performed to include all patients who had undergone CEHE for choledochal cysts in our institute between April 2005 and February 2012. A total of 19 patients were identified in this study and all patients provided informed consent. The clinical characteristics of all patients are shown in Table 1. The types of choledochal cyst in the present study were type I (no intrahepatic bile duct [IHBD] dilatation) and type IV-A (association with IHBD dilatation) according to Todani's classification.[5] We performed CEHE by open surgery, and intra-operative cholangiography with or without cholangioscopy was used to detect a type of pancreaticobiliary maljunction as well as protein plugs in the residual duct. All patients had a closed suction drain placed at the time of surgery behind the hepaticojejunal anastomosis.

Pancreatitis was diagnosed when more than two of the following signs were present: A documented episode of epigastralgia, hyperamylasemia or hyperlipasemia (the

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upper limit of normal of the serum amylase and lipase values in our institute is 159 and 49 U/L, respectively), and abnormal findings associated with pancreatitis employing a CT scan, ultrasonography, or magnetic resonance cholangiopancreatography.

The amylase and lipase values in drainage and the output of the effluent were measured at 1 post-operative day (POD), 3 or 4 POD (3/4 POD), and between 5 and 7 POD (5-7 POD).

We quantified the incidence of pancreatic leak, defined as any measurable output at or after 3 POD from an operatively placed drain with an amylase and/or lipase content >3 times the upper normal serum value (477 and 147 U/L, respectively), according to an international study group definition.[6]

RESULTS

Pancreatic leak was found in 6 of 19 patients (31.6%). In the pancreatic-leak-present group, the mean age at the operation was higher, and more IV-A type choledochal cysts were included than in the pancreatic-leak-absent group. Five of the six patients with pancreatic leak presented with acute pancreatitis pre-operatively, and two of them developed post-operative pancreatitis [Table 1]. The daily drain output of 19 patients undergoing CEHE for choledochal cysts was measured, and it did not differ between the pancreatic-leak-present and -absent groups [Table 2].

Mean drain amylase value (7,191 U/L) and mean lipase value (15,421 U/L) at 1 POD in the post-operative pancreatitis (+) group were elevated significantly compared to those (201 and 980 U/L, respectively) in the post-operative pancreatitis (−) group [Figures 1 and 2]. They then rapidly fell, and there was little difference in the values at 3/4 and 5-7 POD between post-operative pancreatitis (+) and (−) groups.

Table 1: Clinical characteristics of patients with CC

Clinical characteristics	All patients	Pancreatic leak	
		Absent	Present
No. of patients	19	13	6
Age (m)			
Mean	39.7	45.7	72.0
Range	0-186	0-186	33-176
Sex			
Male	10	6	4
Female	9	7	2
Type of CC[a]			
I	12	10	2
IV-A	7	3	4
Shape of CBD dilatation			
Cystic	16	11	5
Fusiform	3	2	1
Pre-operative pancreatitis			
Present	6	1	5
Absent	13	12	1
Prenatal diagnosis	2	2	0
Pre-operative management	1	1 (biliary drainage)	0
Post-operative pancreatitis			
Present	2	0	2
Absent	17	13	4

[a]Todani's classification was used. CBD: Common bile duct; CC: Choledochal cyst

Table 2: Comparison of output in the drainage

	POD	Pancreatic leak			
		Absent (n = 13)		Present (n = 6)	
		Mean ± SD	N	Mean ± SD	N
Output in the drainage (ml/24 h)	1	38.4±38.7	13	46.0±49.9	6
	3/4	13.6± 8.5	12	25.7±18.3	6
	5-7	9.3±6.1	8	21.8±19.4	6

POD: Post-operative day; SD: Standard deviation

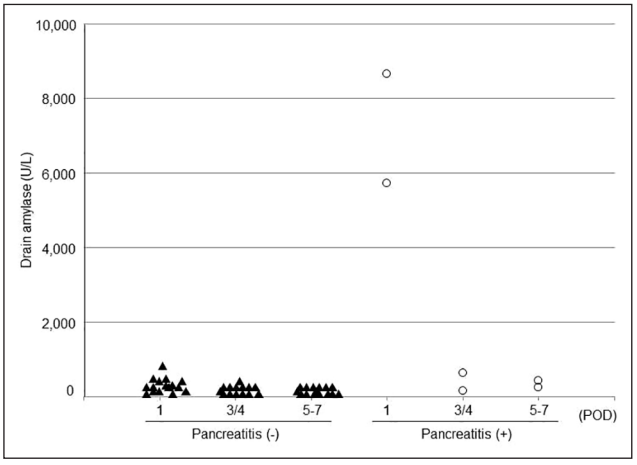


Figure 1: Post-operative change in amylase values in drainage on comparing post-operative pancreatitis (+) to (−) group

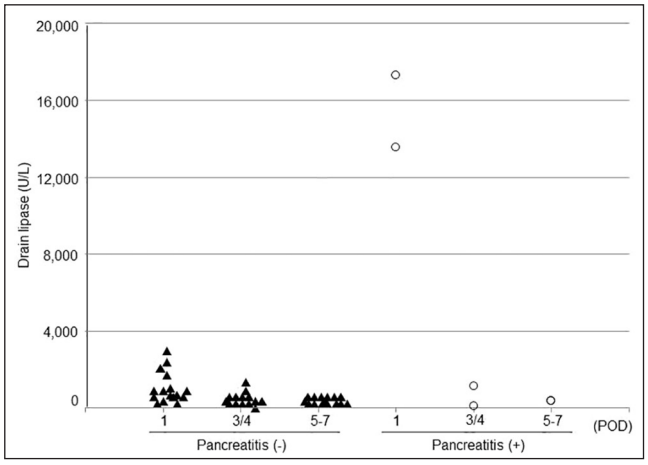


Figure 2: Post-operative change in lipase values in drainage on comparing post-operative pancreatitis (+) to (−) group

Table 3: Post-operative amylase and lipase values in the drainage and serum in patients with a pancreatic leak

Patient			D-amylase (U/L) (POD)			D-lipase (U/L) (POD)			Maximum post-operative value (U/L)		Removal of drain (POD)
No.	Age (m)	Gender	1	3/4	5-7	1	3/4	5-7	S-Amylase	S-Lipase	
Post-operative pancreatitis (+)											
P1	48	Male	5,730	645	259	13,550	1,160	392	1,120	1,480	27
P2	176	Male	8,652	155	430	17,293	113	396	1,494	1,719	10
Post-operative pancreatitis (−)											
N1	33	Female	102	29	31	382	148	12	61	16	7
N2	39	Female	533	373	76	3,420	1,555	380	318	810	11
N3	58	Male	240	116	77	203	130	149	355	223	8
N4	78	Male	103	194	50	60	647	18	131	26	6

POPE: Post-operative pancreatic fistula; POD: Post-operative day; D: Drain; S: Serum. numbers underlined indicate values beyond the upper normal limit

The raw amylase and lipase data for the 6 patients with a pancreatic leak are shown in Table 3. Both drain amylase and lipase values at 1 POD were much higher in the post-operative pancreatitis (+) group versus the (−) group. One patient without post-operative pancreatitis showed a slightly elevated amylase value in drainage; however, the remainder of the patients in the post-operative pancreatitis (−) group showed drain amylase levels within normal limits. In contrast, the lipase value in drainage was beyond the upper limit of the normal range in all patients with a pancreatic leak. In four of them, it was high even at or after 5-7 POD.

Post-operative hyperamylasemia and/or hyperlipasemia was noted in four of the six patients with a pancreatic leak. The patients with post-operative pancreatitis exhibited a prolonged elevation of both serum pancreatic enzymes associated with the activity of pancreatitis, whereas the patients without post-operative pancreatitis showed a transient elevation of the values at 1 POD, which immediately improved.

DISCUSSION

To the best of our knowledge, this is the first study to evaluate the amylase and lipase values in drainage after CEHE for choledochal cysts in order to predict post-operative pancreatitis. Both amylase and lipase values in drainage were markedly elevated at 1 POD in the patients who developed post-operative pancreatitis. The drain amylase value seemed to elevate rather specifically dependent on the occurrence of post-operative pancreatitis, compared with the lipase value, which tended to elevate regardless of the presence/absence of pancreatitis. The number of patients in the present study was so small that we could not define a cut-off value of drain amylase and lipase to identify patients at high risk of developing post-operative pancreatitis. Nevertheless, considering the results of this study, the amylase and lipase values in drainage on the 1 POD were considered to be effective predictors of post-operative pancreatitis, which will be verified by performing a large scale trial.

As shown in the present study, four out of the 19 patients who underwent CEHE for choledochal cysts showed high amylase and/or lipase values in drainage in spite of the fact that they did not develop post-operative pancreatitis. It is speculated that they experienced a capillary leak from the raw pancreatic surface due to intra-operative abrasion of the pancreatic capsule, resulting in a transient but slight elevation of the pancreatic enzymes in the drainage. Three of them presented with acute pancreatitis pre-operatively, suggesting that the occurrence of pre-operative pancreatitis influenced their vulnerability to a capillary leak by means of damage to the weak pancreatic parenchyma with inflammatory changes. In contrast, the extensively high values in drain amylase and lipase found in the two patients with post-operative pancreatitis were considered to have resulted from an enzyme-rich effusion produced by pancreatic auto-digestion. These two disease processes, capillary leak and pancreatic auto-digestion, are completely different from each other in terms of the severity of the clinical course, reflected by the necessity of aggressive management to prevent exacerbation. The present study suggests that it may be possible to predict post-operative pancreatitis at 1 POD by analysis of the drain amylase and lipase values, by which the patient may benefit from lengthening the time of intensive post-operative therapy, such as fluid resuscitation, pain management, and nutritional support.

Interestingly, the drain lipase value was beyond the upper limit of the normal range more frequently and for a longer period after the operation than that of amylase in the absence of post-operative pancreatitis. In contrast, several studies have reported a negative predictive value of serum lipase on diagnosing acute

pancreatitis, between 94% and 100%,[7,8] concluding that serum lipase is the more accurate test in the presence of acute pancreatitis than serum amylase. It may reflect the fact that the half-life of lipase in plasma is longer and its activity remains increased for longer than that of amylase.[9] Moreover, the secretion of both amylase and lipase is low in infants, and adult levels of these enzymes are not reached in the duodenum until late in the 1st year of life.[10] That is why it can be difficult to detect pancreatitis in infants by means of measuring serum pancreatic enzymes. Nevertheless, we encountered five infant patients in the present study, and three of them showed a drain lipase elevation of between 888 and 2,772 U/L at 1 POD, with a normal value of amylase. None of them developed post-operative pancreatitis; however, measuring the drain amylase and lipase values in infants may be more useful to detect the presence of post-operative pancreatitis than those in the serum, if it occurs.

CONCLUSIONS

The present study indicates that post-operative pancreatitis after CEHE for choledochal cysts in children could be predicted by measuring the amylase and lipase values in drainage on the 1 POD. A larger trial is necessary to decide on a cut-off value of drain amylase and lipase to identify patients at high risk of developing post-operative pancreatitis.

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