The Effectiveness of Emergency Endoscopic Retrograde Cholangiopancreatography in Patients with Severe Acute Cholangitis

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ABSTRACT

Background: *Acute cholangitis varies in severity from a mild form responding to antibiotics alone to a severe from requiring urgent decompression of the biliary system. Management of acute biliary infections according to severity grade is also critical, because the urgency of treatment and patient outcomes differ according to the severity of the disease. The aim of this study was to assess the frequency, indications, yield and outcome of emergent endoscopy retrograde cholangiopancreatography (ERCP) in severe acute cholangitis patients.*

Method: *Records of all cholangitis patients undergoing ERCP were reviewed over a six months period. Indications, findings, therapeutic interventions and survival were analyzed. Indications for urgent drainage were temperature greater than 38ºC, increasing abdominal pain, jaundice and any organ involvement.*

Results: *Of 80 ERCPs, 19 (23.75%) were severe acute cholangitis patients underwent emergency ERCP. The common bile duct was the duct of interest in all patients and was cannulated in 100%. The most common findings were choledocholithiasis (42.1%) and pancreatic head cancer (42.1%), followed by cholangiocarcinoma (10.5%) and papil vater carcinoma (5.3%). There were 12 (63.2%) septic shock patients with systolic blood pressure less than 90 mmHg and heart rate greater than 90 beats/minute who required inotropic drugs. Endoscopic biliary drainage was performed using 8.5 F biliary stent (73.7%) or common bile duct (CDB) stones removal (26.3%). The overall 30 days mortality was 0.*

Conclusion: *Emergency ERCP in severe acute cholangitis is associated with improvement of clinical and some laboratory parameters without a complication of acute pancreatitis. In cases of chIoledocholithiasis, it can be performed with stone extraction as well as stent insertion*

Keywords: *severe acute cholangitis, emergent ERCP, endoscopic stenting in difficult hilar biliary stricture*

INTRODUCTION

Acute cholangitis progresses from local biliary infection to the systemic inflammatory response syndrome (SIRS), and advanced disease leads to sepsis with or without organ dysfunction.[1] Acute cholangitis varies in severity from a mild form responding to antibiotics alone to a severe form requiring urgent decompression of the biliary system. It has been reported that when no appropriate biliary drainage was available 20–30 years ago, the mortality of acute cholangitis with conservative treatment was extremely high.[2] The mortality for acute cholangitis has decreased from 100% to around 9-40% with the introduction of antibiotics and biliary decompression. Intravenous (i.v.) antibiotics nowadays are the first-line treatment for acute cholangitis. For those who fail to respond to conservative management, urgent biliary tract decompression should be undertaken. This is the group of patients in whom mortality was often high in the 1970s and 1980s: around 13-88%.

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Urgent decompression is recommended for patients with the classic Charcot's triad of pain, fever and jaundice accompanied by hypotension and mental confusion.[3] For those without the above features, however, it is not always easy to determine at an early stage which patients will respond to medical treatment and which will require urgent biliary decompression.[4]

In 2007, there was a guidelines management of cholangitis and cholecystitis or known as Tokyo Guidelines. Patients with acute cholangitis and organ failure are classified as having severe or grade III acute cholangitis. These patients require organ support, such as ventilatory/circulatory management (eg. endotracheal intubation, artificial respiration management, and the use of vasopressin), and treatment for disseminated intravascular coagulation (DIC) in addition to the general medical management. Urgent biliary drainage must be anticipated. When the patient is stabilized, urgent endoscopic or percutaneous transhepatic biliary drainage or an emergency operation with decompression of the bile duct with a T-tube should be performed. Definitive treatment of the cause of the obstruction, including endoscopic, percutaneous, or operative intervention, should be considered once the acute illness has resolved.[5]

In this study, we undertaken the effectiveness of emergency endoscopy retrograde cholangio-pancreatography (ERCP) in patients with severe cholangitis in Hasan Sadikin hospital, Bandung before Tokyo guidelines was published.

METHOD

This is a retrospective review of patients with severe cholangitis presenting to Hasan Sadikin hospital from July to December 2006. All patients > 14 years old with symptom of jaundice, right upper quadrant abdominal pain and fever were recruited to this study. Inclusion criteria: (1) Hyperbilirubinemia (conjugated hyperbilirubinemia); (2) Leukocytosis or leucopenia; (3) Elevated gamma GT and alkaline phosphatase; (4) Dilated of intrahepatic and or extrahepatic biliary duct proven by sonography or magnetic resonance cholangiopancreatography (MRCP); (5) Organ dysfunctions based on Tokyo guidelines. Exclusion criteria: (1) Unconjugated hyperbilirubinemia; (2) Patients who refused for ERCP procedure.

Patients who diagnosed clinically with acute cholangitis were managed in emergency room (ER) of Internal Medicine Department of Hasan Sadikin hospital. Medical management were done in ER and followed by therapeutic ERCP. Hemodynamic stabilization was done prior to ERCP. In this study, we analyzed the successful rate emergency ERCP in laboratory parameters changes.

All statistical analyses were performed using software statistical program for social sciences (SPSS) version 15.0 for windows. Univariate analysis performing frequency and percentage of the data were done descriptively. Mann Whitney test was used to continuous variables and skewed distribution. Statistical significance was defined as $p \leq 0.05$.

RESULTS

Out of 80 patients underwent ERCP procedures in Endoscopy Unit at Division of Gastroentero-hepatology, Internal Medicine Department, Hasan Sadikin hospital; therewere 19 patients fulfilled the inclusion criteria. Only 4 (21.1%) patients were under 40 years old, the rest were older. A male to female ratio is 11 : 8. Eight (42.1%) patients had biliary stones, 8 (42.1%) patients had pancreatic head carcinoma, 2 (10.5%) patients had cholangiocarcinoma and 1 (5.3%) patient had ampullary carcinoma. Episode of shock was experienced in 12 (63.2%) patients. Of these patients, biliary stent insertion was performed in 14 (73.3%) patients and stone extraction in 5 (26.3%). Demographic data of the patients are shown in table 1.

Table 1. Demographic data of patient

Variable	n	%
Sex		
Male	11	57.9
Female	8	42.1
Age (years old)		
< 40	4	21.1
40 – 49	4	21.1
50 – 59	6	31.5
60 – 69	5	26.3
Etiology		
Choledocholithiasis	8	42.1
Pancreatic head carcinoma	8	42.1
Cholangiocarcinoma	2	10.5
Ampullary carcinoma	1	5.3
Episode of shock		
Yes	12	63.2
No	7	36.8
Therapeutic intervention		
Biliary stent insertion (8.5 Fr)	14	73.7
Stones extraction	5	26.3

There were significantly differences between some laboratory parameters before and after ERCP, using Wilcoxon test with CI 95%. They were leukocytes ($p = 0.026$), total bilirubin ($p = 0.001$), direct bilirubin ($p = 0.001$), alanine aminotransferase (ALT)

Table 2. Differences of laboratory parameters before and after ERCP

Laboratory parameters	Mean		p*
	Before ERCP	After ERCP	
Leukocyte (cells/μL)	13,902.11 (7,174.49)	9,037.37 (5374.85)	0.026
Total bilirubin (mg/dL)	16.41 (11.70)	7.36 (8.48)	0.001
Direct bilirubin (mg/dL)	11.30 (7.80)	5.54 (6.61)	0.001
Urea N (mg/dL)	85.88 (72.34)	35.13 (18.45)	0.093
Creatinine (mg/dL)	2.40 (1.81)	0.97 (0.54)	0.083
Random blood sugar (mg/dL)	153.75 (79.94)	145.50 (80.91)	0.532
Sodium (mEq/L)	137.50 (4.72)	137.66 (4.96)	0.953
Potassium (mEq/L)	3.78 (0.49)	3.41 (0.55)	0.360
AST (IU/L)	112.93 (52.85)	73.06 (70.58)	0.051
ALT (IU/L)	108.86 (82.03)	43.86 (22.52)	0.010
Alkaline phosphatase (IU/L)	421.87 (196.63)	330.25 (197.48)	0.020
Amylase (unit/L)	107.00 (79.04)	78.40 (52.88)	0.358
Lipase (unit/L)	184.20 (305.41)	120.51 (81.82)	0.521

*) Wilcoxon test

Table 3. Differences of laboratory parameter changes in patients who underwent stone extraction and stent insertion

Laboratory parameters	Procedure (mean)		p*
	Stone extraction	Stent insertion	
Hemoglobine (g/dL)	0.58 (0.27)	2.59 (3.12)	0.057
Leukocyte (cells/μL)	9,140.00 (7005.56)	3,337.85 (9,016.86)	0.308
Hematocrit	2.20 (3.03)	5.28 (4.99)	0.285
Platelet (/mL)	71,561.8 (159,888.47)	27,358.2 (102,012.15)	0.711
Total bilirubin (mg/dL)	8.73 (5.86)	9.18 (9.29)	0.916
Direct bilirubin (mg/dL)	6.28 (3.44)	5.53 (6.24)	0.833
Urea N (mg/dL)	141.00 (0.00)	37.85 (69.29)	0.275
Creatinine (mg/dL)	4.04 (0.00)	1.05 (1.83)	0.127
AST (IU/L)	64.75 (75.43)	30.81 (72.87)	0.661
ALT (IU/L)	62.00 (57.78)	66.09 (94.24)	0.753
Alkaline phosphatase (IU/L)	112.75 (211.95)	84.58 (121.78)	0.467
Amylase (unit/L)	5.00 (50.64)	44.33 (115.66)	0.670
Lipase (unit/L)	217.93 (495.22)	13.43 (101.57)	0.504

*) Mann Whitney test

($p = 0.010$), and alkaline phosphatase ($p = 0.020$). The rest of laboratory parameters were not significant in change before and after ERCP, including amylase and lipase ($p = 0.358$ and 0.521). Using a statistic test of Mann Whitney test with CI 95% showed no statistically significant in differences of laboratory parameter changes between patient who underwent stone extraction procedure nor stent insertion procedure.

DISCUSSION

Management of acute biliary infections according to severity grade is also critical, because the urgency of treatment and patient outcomes differ according to the severity of the disease.[6] The decision to intervene in acute cholangitis depends on the clinical findings of progression of the disease or failure to respond to medical treatment. The operative mortality of 20-40% in this group may be due to the often sudden clinical deterioration and the therapeutic intervention involved. On the other hand, urgent intervention in all patients with acute cholangitis is not necessary and is not always feasible.[3] Although endoscopic drainage is less invasive than other drainage techniques and should be considered as the drainage technique of first choice, details of its procedures remain controversial.[7] Results of Tokyo consensus meeting for severe acute

cholangitis mentioned that biliary drainage must be done as soon as possible or emergency and panelists agreed that either endoscopic nasobiliary drainage (ENBD) or biliary tube stent placement could be used.[2]

As patients with severe acute cholangitis have a higher mortality, it would be more prudent to choose a cut-off score with a higher sensitivity in order to institute appropriate treatment earlier. With the early relief of obstruction, septicaemic shock may be prevented and, indeed, patients requiring inotropic support were associated with a higher mortality. Furthermore, endoscopic biliary drainage in patients with septicaemic shock entails a mortality of 4.7 ± 10%. Therefore, it would be more desirable to identify groups of patients in advance so that urgent decompression could be performed when they were still haemodynamically stable and without coagulopathy.[3]

According to American Society for Gastrointestinal Endoscopy (ASGE) guideline, endoscopic retrograde cholangiopancreatography (ERCP) appears to be > 90% sensitive for the detection of choledocholithiasis and offers the potential for therapeutic intervention. However, there is a 3-6% complication rate associated with therapeutic ERCP for stone removal. Percutaneous transhepatic cholangiography (PTC) appears to be as effective for diagnosis and therapy of choledocholithiasis as ERCP, but it has a lower success rate in patients without a dilated biliary tree and may require more than one procedure. When choledocholithiasis is suspected, the use of ERCP or PTC should depend largely on local expertise.[8]

Poon et al showed that an aggressive policy of early endoscopic biliary drainage has resulted in a low mortality rate of 1.7%, which comprised predominantly elderly patients. Expeditious decompression of the biliary tree is particularly important to prevent mortality in elderly patients compromised by comorbid illnesses, who could decompensate quickly in the face of sepsis. A recent study has shown that delay in ERCP in patients with severe cholangitis resulted in increased mortality and morbidity.[9]

Salek et al did a study of the factors that can be used to predict mortality and the need for early ERCP in patients with acute cholangitis. They found that total bilirubin ($p < 0.01$), partial prothrombin time ($p < 0.01$), and presence of a liver abscess ($p < 0.01$) were found to be significant in predicting mortality. Alanine aminotransferase ($p < 0.01$) and white blood cell count ($p < 0.01$) were determined to be predictive of a need for early ERCP.[10] In our study, we found improvement of leukocyte ($p = 0.026$), total and direct bilirubin ($p = 0.001$), alkaline phosphates ($p = 0.020$) and ALT ($p = 0.010$) after emergency ERCP. There were no evidence of elevated serum amylase nor lipase after ERCP in both intervention, stone extraction and stent insertion.

CONCLUSION

Emergency ERCP in severe acute cholangitis is associated with improvement of clinical and some laboratory parameters without a complication of acute pancreatitis. In cases of choledocholithiasis, it can be performed with stone extraction as well as stent insertion.

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