

Endoscopic management of acute cholangitis in elderly patients

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Abstract

AIM: To evaluate clinical presentation, etiology, complications and response to treatment in elderly patients with acute cholangitis.

METHODS: Demographics, etiology of biliary obstruction, clinical features, complications and associated systemic diseases of 175 patients with acute cholangitis were recorded. Endoscopic biliary drainage was performed using nasobiliary drain or stent. The complications related to ERCP, success of biliary drainage, morbidity, mortality and length of hospital stay were evaluated.

RESULTS: Of 175 patients, 52 aged ≥ 60 years (group I, age < 60 years; group II, age ≥ 60 years) and 105 were men. Fever was present in 38 of 52 patients of group II compared to 120 of 123 in group I. High fever (fever $\geq 38.0^{\circ}\text{C}$) was more common in group I (118/120 vs 18/38). Hypotension (5/123 vs 13/52), altered sensorium (3/123 vs 19/52), peritonism (22/123 vs 14/52), renal failure (5/123 vs 14/52) and associated comorbid diseases (4/123 vs 21/52) were more common in group II. Biliopancreatic malignancy was a common cause of biliary obstruction in group II ($n = 34$) and benign diseases in group I ($n = 120$). Indications for biliary drainage were any one of the following either singly or in combination: a fever of $\geq 38.0^{\circ}\text{C}$ ($n = 136$), hypotension ($n = 18$), peritonism ($n = 36$), altered sensorium ($n = 22$), and failure to improve within 72 h of conservative management ($n = 22$). High grade fever was more common indication of biliary drainage in group I and hypotension, altered sensorium, peritonism and failure to improve within 72 h of conservative management were more common indications in group II. Endoscopic biliary drainage was achieved in 172 patients (nasobiliary drain: 56 group I, 24 group II, stent: 64 group I, 28 group II) without any significant age related difference in the success rate. Abdominal

pain, fever, jaundice, hypotension, altered sensorium, peritonism and renal failure improved after median time of 5 d in 120 patients in group I (2-15 d) compared to 10 d in 47 patients of group II (3-20 d). Normalization of leucocyte count was seen after a median time of 7 d (3-20 d) in 120 patients in group I compared to 15 d (5-26 d) in 47 patients in group II. There were no ERCP related complications in either group. Five patients (carcinoma gallbladder $n = 3$, CBD stones $n = 2$) died in group II and they had undergone biliary drainage after failure of response to conservative management for 72 h. There was a higher mortality in patients in group II despite successful biliary drainage (0/120 vs 5/52). Length of hospital stay was longer in group II patients (16.4 ± 5.6 , 7-30 d) than in group I patients (8.2 ± 2.4 , 7-20 d).

CONCLUSION: Elderly patients with acute cholangitis have a high incidence of severe cholangitis, concomitant medical illnesses, hypotension, altered sensorium, peritonism, renal failure and higher mortality even after successful biliary drainage.

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Key words: Acute cholangitis; Endoscopic biliary drainage; Endoscopic retrograde cholangio-pancreatography; Common bile duct stones; Carcinoma gall bladder

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INTRODUCTION

Acute cholangitis is a difficult diagnostic and therapeutic problem. Classically, Charcot's triad of jaundice, abdominal pain and fever have been the main basis of diagnosis however 30%-45% of the patients with acute cholangitis do not satisfy the criteria of Charcot's triad^[1].

Altered sensorium, hypotension and renal failure can often be seen in patients with suppurative cholangitis^[2]. In many cases, bile duct infection is latent and does not cause symptoms. Cholangitis varies in severity from a mild form which responds to parenteral antibiotics alone to severe or suppurative cholangitis which requires early drainage of biliary system to reduce the incidence of

systemic complications^[3]. Endoscopic biliary drainage is an established mode of treatment for acute cholangitis with high success rate, low morbidity and mortality^[1,3-20].

Old age is considered as a risk factor associated with significant mortality in acute cholangitis^[21,22]. It is also a factor which adversely affects the outcome and survival in patients with acute cholangitis, which may be due to associated other systemic diseases and comorbid conditions, underlying etiology of biliary obstruction, poor immune status and poor general health in old age^[21-23]. However, there is no study on clinical presentation, etiology, complications and survival after endoscopic biliary drainage in elderly patients with acute cholangitis. We prospectively compared the clinical presentation, etiology, associated systemic diseases, complications and response to treatment in elderly patients with acute cholangitis.

MATERIALS AND METHODS

Over past 5 years, 175 patients with acute cholangitis were recruited in this study. The diagnosis of acute cholangitis was based on presence of clinical evidence of infection (fever, leucocytosis and abdominal pain) in patients with biliary obstruction in the form of jaundice or hyperbilirubinemia^[1,3]. Patients with biliary obstruction and associated hypotension, impaired level of consciousness and renal failure were specifically looked for associated features of acute cholangitis like fever and leucocytosis. They were labelled to be having acute cholangitis if they had any of features like hypotension, impaired level of consciousness and renal failure along with fever and /or leucocytosis in absence of infection at other sites or other causes for hypotension, impaired level of consciousness and renal failure. Details of demographic data, etiology of biliary obstruction, clinical features, biochemical parameters, microbiological spectrum, complications and associated other systemic diseases were recorded.

Immediate endoscopic biliary drainage was performed in patients with high fever, hypotension, peritonism, altered sensorium and associated renal failure. In patients without these features, endoscopic biliary drainage was performed only if they did not respond to conservative treatment. All patients were treated with intravenous antibiotics and metronidazole. Concomitant medical illnesses were also recorded and treatment was started to control these medical illnesses. Endoscopic retrograde cholangiopancreatography (ERCP) was performed with a side viewing duodenoscope with a large accessory channel in a standard manner. Patients were subjected to either nasobiliary drain (NBD) placement or placement of biliary stent. After cannulation of the common bile duct, bile was aspirated to confirm the position of the cannula. Injection of contrast was avoided as far as possible to prevent any sudden increase in bile duct pressure which could lead to sudden cholangiovenous and cholangiolymphatic reflux. Endoscopic sphincterotomy was not performed. Either a 7-F nasobiliary drain or 7-F straight flap stent was placed in bile duct. After ERCP and biliary drainage, all the patients were kept under strict observation and treated in a critical care ward and the amount of bile drained from

Table 1 Demographic and clinical characteristics of patients with severe acute cholangitis

| | Group I | Group II |
|------------------------------------|-------------------------|--------------------------------------|
| <i>n</i> | 123 | 52 |
| Mean age \pm SD (range) years | 38.6 \pm 12.4 (20-56) | 68.4 \pm 10.8 ^a (60-90) |
| Gender (Male: Female) | 72:51 | 33:19 |
| Clinical presentation <i>n</i> (%) | | |
| Right upper | 116 (94.3) | 27 (52) ^a |
| Quadrant pain | 118 (96) | 18 (34.6) ^a |
| Fever \geq 38.0°C | 2 (1.6) | 20 (38.4) ^a |
| < 38.0°C | 120 (97.5) | 48 (92.3) |
| Jaundice | 3 (2.4) | 19 (36.5) ^a |
| Altered sensorium | 5 (4.0) | 13 (25.0) ^a |
| Hypotension | 22 (17.8) | 14 (11.3) ^a |
| Peritonism | 5 (4.0) | 14 (11.3) ^a |
| Renal failure | 4 (3.2) | 21 (40.3) ^a |
| Other systemic illnesses | | |

^a*P* < 0.05.

NBD was monitored daily.

The patients were closely observed for evidence of ERCP-related complications. Clinical improvement was defined as normalization of fever, leucocytosis, hypotension, peritonism, altered sensorium and renal functions. After clinical improvement, a repeat ERCP or NBD cholangiogram was obtained in each patient. Clinical monitoring and biochemical tests were performed before ERCP and then on d 1, 3 and 7 after ERCP or earlier if indicated. After improvement of their cholangitis, patients underwent some form of definitive management. Primary outcome measures included complications related to ERCP and the treatment outcomes including success of biliary drainage, morbidity, mortality and length of hospital stay.

Statistical analysis

Quantitative data were expressed as the mean \pm SD or as the median. The Mann-Whitney *U* test was used for comparing continuous variables and a Chi-square test with Yate's correction was used to analyze clinical variables and the two tailed Fisher's exact test was used when numbers were small. A *P* value < 0.05 was considered to be statistically significant.

RESULTS

Of 175 patients, 52 patients were aged \geq 60 years (group I, age < 60 years; group II, age \geq 60 years) and 105 were men. Most patients presented with right upper quadrant abdominal pain, jaundice and fever with chills. Of 175 patients, right upper quadrant abdominal pain and fever were more common in group I compared to group II (Table 1). Fever was present in 38 of 52 patients of group II compared to 120 of 123 patients in group I. However, high fever (fever \geq 38.0°C) was more common in patients of group I (118/120 *vs* 18/38) (Table 1). Of 175 patients, hypotension (5/123 *vs* 13/52), altered sensorium (3/123 *vs* 19/52), peritonism (22/123 *vs* 14/52) and renal failure (5/123 *vs* 14/52) were more common in patients of group II compared to patients with group I.

Table 2 Etiology and site of biliary obstruction in common bile duct

| Etiology of biliary obstruction | Site of biliary obstruction | Group I n = 123 (%) | Group II n = 52 (%) |
|----------------------------------|-----------------------------|------------------------|------------------------|
| Benign causes (n = 138) | | | |
| Common bile duct stone | Lower | 104 (84.5) | 18 (34.6) ^a |
| Chronic pancreatitis | Lower | 2 (1.6) | 0 |
| Post operative biliary stricture | Upper | 7 (5.7) | 0 |
| Hydatid cyst rupture | | | |
| with fistula | Upper | 4 (3.2) | 0 |
| Rupture liver abscess | | | |
| with fistula | Upper | 3 (2.4) | 0 |
| Malignant causes (n = 37) | | | |
| Gallbladder carcinoma | Upper | 2 (1.6) | 14 (27) ^a |
| Cholangiocarcinoma | Upper + middle | 0 | 5 (9.6) ^a |
| Periampullary carcinoma | Lower | 1 (0.8) | 15 (28.8) ^a |

Table 3 Laboratory parameters before endoscopic biliary drainage (mean ± SD)

| | Group I (n = 123) | Group II (n = 52) | P |
|---|----------------------|----------------------|--------|
| Total leucocyte count, × 10 ⁹ /L | 28.6 ± 6.4 | 20.4 ± 4.6 | < 0.01 |
| Total bilirubin, mg/dL | 12.4 ± 8.2 | 20.6 ± 10.4 | < 0.01 |
| Aspartate aminotransferase, IU/L | 62 ± 24 | 58 ± 20.6 | NS |
| Alanine aminotransferase, IU/L | 52 ± 18.4 | 56 ± 14.4 | NS |
| Alkaline phosphatase, IU/L | 402 ± 196 | 1126 ± 644 | < 0.01 |
| Serum albumin, g/dL | 3.6 ± 0.8 | 3.8 ± 0.8 | NS |

Some patients in group II presented with hypotension or altered sensorium despite no or mild abdominal pain and low grade fever.

Etiology and site of biliary obstruction in 175 patients are summarized in Table 2. The biliopancreatic malignancy was a common cause of biliary obstruction in patients of group II (n = 34) compared to benign diseases in group I (n = 120) (Table 2).

Of 175 patients, 25 patients had other associated comorbid systemic conditions (group I, n = 4 and group II, n = 21) like diabetes mellitus (n = 10), hypertension (n = 12), coronary artery disease (n = 6), cerebrovascular accidents (n = 4), chronic obstructive pulmonary disease (n = 4) and pulmonary tuberculosis (n = 3) in group II patients compared to pulmonary tuberculosis (n = 2), rheumatic heart disease (n = 1), diabetes mellitus (n = 1), hypertension (n = 1) and thyrotoxicosis (n = 1). Laboratory investigation revealed higher elevation of leucocytes in group I and higher elevations of bilirubin and alkaline phosphatase levels in group II patients (Table 3). Blood cultures were positive in 70 cases (40%, group I, n = 50; group II, n = 20) with organisms such as *Escherichia Coli* (n = 50; group I, n = 38; group II, n = 12), *Klebseilla* (n = 12; group I, n = 9; group II, n = 3), *Acinobacter* (n = 13; group I, n = 9; group II, n = 4), *Proteus* (n = 9; group I, n = 6; group II, n = 3) and *Pseudomonas* (n = 9; group I, n = 6; group II, n = 3). Twenty-three patients had mixed infections. The biliary obstruction was most commonly found to be in the lower part of common bile

Table 4 Indications of biliary drainage

| Indication | Group I n = 123 (%) | Group II n = 52 (%) | P |
|---|------------------------|------------------------|--------|
| Fever ≥ 38.0°C | 118 (96) | 18 (34.6) | < 0.01 |
| Hypotension | 5 (4) | 13 (25) | < 0.01 |
| Peritonism | 22 (18) | 14 (26.9) | < 0.01 |
| Altered sensorium | 3 (2.6) | 19 (36.5) | < 0.01 |
| Failure to improve with conservative management | 2 (1.6) | 20 (38.4) | < 0.01 |

duct in both group I (n = 107) and group II (n = 33) patients. Indications for biliary drainage were any one of the following either singly or in combination: a fever of ≥ 38.0°C (n = 136), hypotension, with systolic blood pressure < 100 mm Hg (n = 18), right upper quadrant abdominal pain with guarding (peritonism) (n = 36), impaired level of consciousness (n = 22), and failure to improve within 72 h of conservative management (n = 22). High grade fever was more common indication of biliary drainage in group I and hypotension, altered sensorium, peritonism and failure to improve within 72 h of conservative management were more common indications of biliary drainage in group II patients (Table 4). None of the patients had undergone prior endoscopic or percutaneous transhepatic biliary drainage. After hospital admission, ERCP and endoscopic biliary drainage were performed in patients with severe acute cholangitis after a median interval of 20 h (range 3-42 h) in 153 patients and after a median interval of 96 h (range 72-106 h) in 22 patients who failed to respond to conservative management.

Endoscopic biliary drainage was achieved in 172 patients without any significant age related difference in the success rate. A nasobiliary drain was placed in 80 patients (56 group I, 24 group II) and a stent was placed in 92 patients (64 group I, 28 group II). ERCP with biliary drainage therefore could be achieved in 120 patients in group I and 52 patients in group II. Abdominal pain, fever, jaundice, hypotension, altered sensorium, peritonism and renal failure improved after median time of 5 d in all the 120 patients in group I (range 2-15 d) and after median time of 10 d in 47 patients of group II (range 3-20 d). Similar normalization of leucocyte count was seen after a median time of 7 d (range 3-20 d) in 120 patients in group I and after a median time of 15 d (range 5-26 d) in 47 patients in group II. There were no immediate ERCP related complications in either group of patients. There were no episodes of displacement, kinking or occlusion of NBD or of occlusion or migration of stent.

Five patients (carcinoma gallbladder n = 3, CBD stones n = 2) died in group II after 3, 5, 6, 9 and 10 d of endoscopic biliary drainage. All the five patients were subjected to endoscopic biliary drainage (2 NBD, 3 stent) after they failed to respond to conservative management for 72 h. All the five patients died because of uncontrolled cholangitis and septicemia despite antibiotics and successful endoscopic biliary drainage.

There was a higher mortality in patients in group II despite successful biliary drainage (0/120 vs 5/52). There was no significant difference in mortality between group

Table 5 Clinical characteristics, indications and results of biliary drainage in patients with acute cholangitis due to stones in common bile duct ($n = 122$)

| | Group I $n = 104$ (%) | Group II $n = 18$ (%) | <i>P</i> |
|--|--------------------------|--------------------------|----------|
| Clinical parameters | | | |
| Fever | 102 (98) | 10 (55.5) | < 0.01 |
| Jaundice | 101 (97.1) | 14 (77.7) | < 0.01 |
| Altered sensorium | 1 (0.96) | 8 (44.4) | < 0.01 |
| Hypotension | 1 (0.96) | 5 (27.8) | < 0.01 |
| Peritonism | 12 (11.5) | 6 (33.3) | < 0.01 |
| Renal failure | 3 (2.8) | 7 (38.9) | < 0.01 |
| Indications of biliary drainage | | | |
| Fever $\geq 38.0^{\circ}\text{C}$ | 102 (98) | 6 (33.3) | < 0.01 |
| Hypotension | 1 (0.96) | 5 (27.8) | < 0.01 |
| Peritonism | 12 (11.5) | 6 (33.3) | < 0.01 |
| Altered sensorium | 1 (0.96) | 8 (44.4) | < 0.01 |
| Failure to improve with conservative treatment | 1 (0.96) | 7 (38.9) | < 0.01 |
| Results of biliary drainage | | | |
| Time taken for improvement | | | |
| Median (range) days | 5 (2-15) | 10 (3-20) | < 0.01 |
| Mortality | 0 | 2 | < 0.01 |
| Length of hospital stay | | | |
| Mean (range) days | 8.2 (7-20) | 16.4 (7-30) | < 0.01 |

II patients with (2/21) and without (3/31) concurrent diseases. Also there was no difference in mortality between group II patients with benign (2/18) and malignant causes (3/34) of biliary obstruction. Length of hospital stay was significantly longer in group II patients (16.4 ± 5.6 , range 7-30 d) than in group I patients (8.2 ± 2.4 , range 7-20 d). Altered sensorium, hypotension, peritonism, mortality and length of hospital stay were more in group II patients with CBD stones ($n = 18$) than in group I patients with CBD stones ($n = 104$) (Table 5).

DISCUSSION

Older age has been considered a risk factor for increased morbidity and mortality rates in the treatment of acute cholangitis^[21,22]. However there is little specific information available on clinical features and treatment of acute cholangitis in the elderly. In present study elderly patients with acute cholangitis were found to have relatively higher incidence of severe cholangitis, hypotension, altered sensorium, peritonism and renal failure. Symptoms in elderly patients did not correlate with the severity of acute cholangitis. Many elderly patients with severe cholangitis presented with deceptively mild symptoms. Presence of abdominal pain and high grade fever was less common in elderly patients compared to young patients. Almost 40% of elderly patients had low grade fever and nearly ¼ did not have fever. Therefore early diagnosis of acute cholangitis based on symptoms alone was difficult as reported earlier^[21]. However on examination many elderly patients had features suggestive of severe cholangitis in form of jaundice, hypotension, altered sensorium, peritonism and associated renal failure. All the elderly patients showed abnormal results of laboratory tests. However rise in leucocyte count was less compared to leucocytosis in younger patients and bilirubin and alkaline

phosphatase levels were higher in elderly patients than in younger patients. This could be due to biliopancreatic malignancy, a common cause of biliary obstruction in elderly patients compared to benign diseases in younger patients. Elderly patients also had a higher incidence of coexisting medical problems like cardiovascular, pulmonary, neurological and other systemic diseases. Due to the high incidence of severe cholangitis, features like hypotension and altered sensorium and associated other concurrent systemic diseases, the management of acute cholangitis in the elderly becomes difficult^[21].

Urgent endoscopic biliary drainage has been recommended for severe acute cholangitis or cholangitis that does not respond to conservative treatment^[1,3-20]. Endoscopic biliary drainage including endoscopic sphincterotomy, nasobiliary drainage and stenting has been advocated as safe and effective measure for the treatment of acute cholangitis with a mortality ranging from 2% to 8%. In present series, urgent endoscopic biliary drainage yielded favorable outcome for all the young patients. However endoscopic biliary drainage for elderly patients was associated with significant mortality. Earlier studies have shown that the success rates of therapeutic ERCP are similar between elderly and young patients^[24,25]. However the morbidity and mortality associated with therapeutic ERCP are significantly greater in the elderly than in young patients^[23-25]. There were no serious complications of endoscopic biliary drainage procedures in both elderly and younger patients. In elderly patients higher morbidity and mortality even after biliary drainage are considered due to advanced acute cholangitis, exacerbation of concurrent medical illnesses, unsuccessful biliary drainage procedures, underlying biliopancreatic malignancy as a cause of biliary obstruction, complications characteristic of elderly such as delirium, pneumonia or atelectasis and need for prolonged ventilatory support after the endoscopic drainage procedures^[21-25]. Elderly patients are often unable to tolerate endoscopic procedures because they are critically ill or uncooperative. In this situation, the endoscopic procedures can be performed safely and successfully under general anesthesia and endotracheal intubation^[21,25]. However none of the elderly patients in present series required general anesthesia, endotracheal intubation and ventilatory support after endoscopic procedures for biliary drainage.

In present study, the clinical profile and response to endoscopic biliary drainage in elderly patients was similar in patients having biliary obstruction due to benign and malignant causes. Elderly patients with CBD stones had different clinical profile, poorer response to biliary drainage and higher mortality as compared to young patients with CBD stones. In present series, all the five elderly patients were subjected to endoscopic biliary drainage after they failed to respond to conservative management for 72 h. All the five patients died because of uncontrolled cholangitis and septicemia despite antibiotics and successful endoscopic biliary drainage. None of the patients who underwent immediate endoscopic biliary drainage because of high grade fever or associated features like hypotension, altered sensorium and peritonism had died. It is possible that patients with low grade fever and

without features like hypotension, altered sensorium and peritonism also had severe acute cholangitis which was not clinically evident. Therefore they did not fit into indications of immediate endoscopic biliary drainage without waiting for assessment of response to conservative management for 72 h and accounted for 25% (5/20) of mortality in subgroup of elderly patients not responding to conservative treatment for 72 h. Some of the elderly patients presented with hypotension or altered sensorium despite absent or mild abdominal pain and without or with low grade fever suggesting thereby that elderly patients may have severe acute cholangitis without fever or with low grade fever and should be subjected to immediate endoscopic biliary drainage without waiting for 72 h to assess the response to conservative treatment for 72 h. Higher mortality has earlier been reported in patients with acute cholangitis who fail to respond to antibiotics and therapeutic intervention is performed after 72 h of hospital admission^[23,26]. It has been found that many times it is not always clinically apparent which patients will respond to medical treatment alone and which will require urgent biliary drainage. The mortality rate is high for patients who undergo delayed biliary drainage after failure of medical therapy^[23,26]. In elderly patients, the levels of bilirubin and alkaline phosphatase were significantly higher than in young patients. It has been reported that higher levels of bilirubin and alkaline phosphatase are associated with higher mortality in patients with acute cholangitis^[22]. The differences in clinical profile, laboratory parameters and response to biliary drainage in elderly patients can not be attributed to differences in type of bacteria causing cholangitis because the bacteriological spectrum was similar in elderly and young patients in present study.

Elderly patients with acute cholangitis have a high incidence of severe cholangitis, concomitant medical illnesses, hypotension, altered sensorium, peritonism, renal failure and higher mortality even after successful biliary drainage.

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