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EDITORIAL

Changes over time in treatment for obstructive jaundice

Hideki Aoki

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Abstract

This editorial discusses an article by Peng *et al*. This study reviewed the efficacy and safety of a new approach for treating obstructive jaundice. Although the pathophysiology of obstructive jaundice has not yet been fully elucidated, progress has been made in its management. There are two aspects of obstructive jaundice: Cholestatic status and absence of bile in the intestinal lumen. Internal biliary drainage resolved both the conditions. Clinically, endoscopic retrograde biliary drainage (ERBD) has replaced percutaneous transhepatic biliary drainage, and ERBD is transitioning to endoscopic ultrasound guided biliary drainage. This editorial briefly explains the mechanism and treatment of obstructive jaundice and the prospects of this new internal biliary drainage technique.

Key Words: Obstructive jaundice; Intestinal permeability; Biliary drainage; Endoscopic retrograde biliary drainage; Endoscopic ultrasound guided biliary drainage

Core Tip: Internal drainage is considered ideal for biliary drainage; endoscopic retrograde biliary drainage (ERBD) has replaced percutaneous transhepatic biliary drainage, and ERBD is transitioning to endoscopic ultrasound guided biliary drainage. This editorial describes longitudinal studies on obstructive jaundice and the prospects for new internal biliary drainage.

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INTRODUCTION

Obstructive jaundice is a long-term challenge for surgeons. Jaundice is associated with significant morbidity and mortality due to septic complications and renal dysfunction[1,2]. Many clinical and experimental studies were conducted in the 1990s to investigate pathophysiology of obstructive jaundice[3,4]; these studies revealed that gut-derived endotoxins play an important role. Patients with jaundice are believed to be immunocompromised, and the impairment of reticuloendothelial cells, particularly Kupffer cells, are involved. Cholestatic status may impair Kupffer cell function, and Kupffer cell dysfunction may allow gut-derived endotoxins to enter systemic circulation[5]. However, it is unclear how and by what pathway these endotoxins invade the human body.

TWO ASPECTS OF OBSTRUCTIVE JAUNDICE

There are two aspects of obstructive jaundice: Cholestatic status and absence of bile in the intestinal lumen. The bile contains bile acids, bile salts, and secretory IgA. Bile acids, bilirubin, drugs, and other substances in bile enter the intestine, are absorbed by enterocytes, and are transported back to the liver. The bile acids delivered to the duodenum are recycled approximately 6-10 times per day, constituting a collective total of 95% of all bile acid recycling. When the biliary system is obstructed, there is a deficit in the enterohepatic circulation of bile. Bile salts and secretory IgA play important roles in gut barrier function[6]. Bile acids inhibit the growth of certain bacteria and exert trophic effects on intestinal mucosa. Oral deoxycholate or lactulose is administered to reduce the absorption of endotoxins, and it appears to protect against renal impairment after surgery. Pain *et al*[7] stated that although no significant difference was noted, one patient and none in the control (n = 35) and treatment groups (n = 35 in lactulose and n = 32 in sodium deoxycholate) developed postoperative renal failure[7]. As for secretory IgA, in normal situation, approximately 36% of the gut microbiota is coated with secretory IgA, whereas during inflammation, this number can increase up to 69%. Secretory IgA is involved in maintaining intestinal homeostasis by neutralizing pathogenic microorganisms and regulating the gut microbiota composition[8].

INTESTINAL PERMEABILITY

Increased intestinal permeability was directly observed in jaundiced patients, especially after surgical intervention, by the lactulose-mannitol test[9]. Before internal biliary drainage such as endoscopic retrograde biliary drainage became widespread, percutaneous transhepatic biliary drainage (PTBD) was the main procedure. External biliary drainage resolves the cholestatic status, and liver dysfunction recovers to some extent. However, the drained bile is abandoned, and the deficit of enterohepatic circulation of bile continues. Some experimental studies have demonstrated the superiority of internal biliary drainage[3,10]. Gouma *et al*[10] reported mortality following peritonitis in rats with obstructive jaundice after relief from internal or external biliary drainage. The mortality rate after internal drainage was significantly lower (25%) than after external drainage (63%)[10]. However, internal biliary drainage was not routinely performed in clinical settings at that time. Clinically, bile replacement during external biliary drainage restores the intestinal barrier function in jaundiced patients by repairing physical damage to the intestinal mucosa. Kamiya *et al*[11] reported that the biliary concentrations of bile acids, cholesterol, and phospholipids significantly increased, and the lactulose-mannitol ratio significantly decreased after bile replacement[11].

INTERNAL BILIARY DRAINAGE

Although some mechanisms have become clear in obstructive jaundice, complications occur at a certain frequency among patients with jaundice, especially after hepatectomy. Therefore, it is essential to improve the condition of patients with jaundice before surgery. Internal biliary drainage resolves cholestasis and bile absence. When endoscopic retrograde cholangiopancreatography (ERCP) fails, PTBD or bypass biliary reconstruction are the only treatment options for treating obstructive jaundice thus far. PTBD is associated with a high rate of complications and dislodgement, and bypass surgery is invasive. In unresectable cases, one report indicated that ERCP was associated with significantly reduced mortality compared with PTBD in patients with pancreatic cancer[12].

In contrast, van der Gaag *et al*[13] revealed that routine preoperative biliary drainage in patients undergoing surgery for pancreatic head cancer increased the rate of complications. The problem was cholangitis after biliary drainage[13]. Drainage was performed mainly *via* endoscopic plastic stent placement. Moreover, in their meta-analysis, Tian *et al*[14] concluded that external drainage is better than internal drainage for malignant biliary obstruction in terms of rate of preoperative cholangitis rate, incidence of stent dysfunction, and total morbidity[14]. They also stated that plastic stents were predominantly used by patients involved. Cholangitis is a problem in patients with cancer undergoing chemotherapy or surgery; therefore, an expandable metallic stent (EMS), which can secure a larger caliber, is becoming the device of choice. In a meta-analysis, Lyu *et al*[15] revealed that the use of EMS in patients with pancreatic cancer undergoing neoadjuvant therapy followed by surgery was associated with lower rates of reintervention, delay of neoadjuvant therapy, recurrent biliary obstruction, and cholangitis than the use of plastic stents. Specifically, the rate of postprocedural cholangitis was 15.4% and 32.5% with EMS and plastic stents, respectively[15]. The clinical guidelines of

the American College of Gastroenterology state that EMS provides significantly longer stent patency and reduces cholangitis events than plastic stents and recommend that EMS be applied to patients with extrahepatic biliary stricture attributable to a resectable malignancy who will undergo preoperative neoadjuvant therapy[16]. However, EMS is associated with a significant range of postprocedural complications, including pancreatitis and cholecystitis, when a covered stent is used.

Endoscopic ultrasound-guided biliary drainage (EUS-BD) using electrocautery-enhanced lumen-apposing metal stents (ECE-LAMs) is a suitable treatment option to resolve these issues. Peng *et al*[17] emphasize a high success rate and low incidence of adverse events, even when performed by nonexperts. However, they mentioned that most of the included studies were retrospective, possibly causing a selection bias. But one distinct advantage of EUS-BD is the significantly reduced rate of postprocedural pancreatitis, which is sometimes lethal. EUS-BD with ECE-LAMS is a palliative treatment option. Although this method has adaptation limitations, it has the potential to become the first choice and is widely used. Furthermore, EUS-BD using ECE-LAMS has been recognized as a bridge-to-surgery approach for planned pancreatoduodenectomies. Chen *et al*[18] conducted a multicenter, randomized controlled study comparing EUS-BD with lumen-apposing metal (LAM) (n = 73) and EMS (n = 71) in patients with malignant biliary obstruction stemming from unresectable, locally advanced, or borderline resectable periampullary cancers. No significant differences were noted in safety, clinical success, or postoperative outcomes; however, EUS-BD with LAM was associated with a significantly shorter procedural time and lower radiation exposure than EMS. EUS-BD is a relatively new technology, and studies on EUS-BD are ongoing. Further investigation, including long-term results, requires large-scale prospective studies.

CONCLUSION

The bile should be returned to the intestine. Internal biliary drainage is ideal both physiologically and cosmetically. This editorial briefly describes these theories.

FOOTNOTES

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