

# Treatment of severe *Clonorchiasis sinensis* by endoscopic nasobiliary drainage and oral praziquantel

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## Abstract

**AIM:** To assess the therapeutic value of endoscopic nasobiliary drainage (ENBD) and oral praziquantel for severe *Clonorchiasis sinensis* infection.

**METHODS:** Of the 84 *Clonorchiasis sinensis*-infected patients enrolled, 58 were treated with ENBD (as observing group, ENBD group), 26 received operations (control group, operation group). Both of the two groups were comparable in terms of patient's age, body mass index. Before and one week after treatment, the average diameters of common bile ducts were measured by ultrasound, and serum bilirubin, ALP,  $\gamma$ -GT and ALT were detected by biochemical methods. After ENBD or operation, the patients took praziquantel for two days.

**RESULTS:** Compared with the patients in operation group, ENBD patients in ENBD group had higher recovery rates of abdominal pain and fever as well as jaundice, quicker remission, smaller trauma, fewer complications and lower cost.

**CONCLUSION:** ENBD combined with oral praziquantel is an effective and safe method for the treatment of severe *Clonorchiasis sinensis*.

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## INTRODUCTION

Oral praziquantel is effective for the treatment of mild *Clonorchiasis sinensis*. As the parasitism of *Clonorchiasis sinensis* metacercaria can take more than 50 years in human body<sup>[1]</sup>, the therapy of *Clonorchiasis sinensis* is very difficult because of repeated infections. We have achieved effective results in treating 58 cases of severe *Clonorchiasis sinensis* infection from July 2000 to April 2003 by endoscopic nasobiliary drainage (ENBD) and oral praziquantel.

## MATERIALS AND METHODS

### Diagnostic criteria for severe *Clonorchiasis sinensis*

Criteria for severe *Clonorchiasis sinensis* are as follows: A

history of eating raw fish; spawn can be detected in feces or bile; obstructive jaundice or cholecystitis, biliary calculus in common bile duct, and suppurative cholangitis. All the 58 cases were in line with the above diagnostic standards.

### Patients and treatments

There were 58 cases in ENBD group including 55 males and 3 females (aged from 29 to 76 with a mean age of 46.5 years). All cases had a history of eating raw fish. Among them, 36 cases had common bile duct dilatation, intrahepatic bile duct and gallbladder distention (6 of the 36 cases also had gallstones in common bile duct); 23 cases had mild dilatation in common bile duct. Nineteen cases were accompanied with fever and increased leukocyte counts. *Clonorchiasis sinensis* metacercaria were detected in feces of 39 cases. Laboratory examination results were as follows: Total bilirubin 86-280  $\mu$ mol/L with an average of 103  $\mu$ mol/L, glutamic-pyruvic transaminase 60-360 U/L with an average of 98 U/L.

The 58 cases in ENBD group were treated according to the routine procedure<sup>[2]</sup>. The instruments included duodenoscope, ducts, knives, guide wires, meshes, etc. The papilla of Vater and bile duct were examined for *Clonorchiasis sinensis* metacercaria. Then, endoscopic retrograde cholangiopancreatography (ERCP) was performed to diagnose the severity of the disease. Patients with mild inflammation without constriction were treated by nasobiliary drainage. Patients with obvious constriction were treated by nasobiliary drainage after sphincterotomy. If the common bile duct was full of *Clonorchiasis sinensis* metacercaria and purulent discharge, the ducts were first washed, and then nasobiliary drainage was performed. For the patients with biliary calculus in common bile ducts, stones were taken out by sphincterotomy followed by nasobiliary drainage. All the 58 patients took praziquantel orally 8-48 h after procedures. The dose was 3.6 g/d three times daily for 2 d.

There were 26 patients with *Clonorchiasis sinensis* infection proved by operations (operation group) including 25 males and 1 female aged 36 to 75 years with a mean age of 48.5 years. Preoperative diagnosis was as follows: Fifteen patients with cholecystitis, 5 with gallstones in common bile duct and 6 with duodenal ampulla carcinoma. Fifteen cases underwent cholecystectomy, 5 cases underwent choledocholithotomy, and 20 cases received operations for common bile duct dilatation. All the 26 cases had T-tube drainage. Laboratory examination results were as follows: Total bilirubin 76-123  $\mu$ mol/L with a mean of 94  $\mu$ mol/L, glutamic-pyruvic transaminase 63-286 U/L with an average of 105 U/L.

The 26 cases were treated by exploratory laparotomy. The common bile duct was opened, and *Clonorchiasis sinensis* metacercaria and their purulent discharge were washed away with saline. Then, common bile duct was expanded with bougie. At last, T-tube was placed inside. Cholecystectomy followed by T-tube was performed for patients with cholecystolithiasis or cholecystitis. Choledocholithotomy followed by T-tube was performed for patients with gallstones in common bile ducts. All the 26 patients took praziquantel orally for 3-6 d after operation. The dose was 3.6 g/d three times daily for 2 d.

**Table 1** Average diameter of common bile ducts, levels of serum total bilirubin, ALP,  $\gamma$ -GT and ALT one week after operation (mean $\pm$ SD)

| Group     | Cases (n) | Therapy | Average diameter of common bile duct (mm) | Serum total bilirubin ( $\mu$ mol/L) | ALP (U/L)                 | $\gamma$ -GT (U/L)       | ALT (U/L)                |
|-----------|-----------|---------|---|--------------------------------------|---------------------------|--------------------------|--------------------------|
| ENBD      | 58        | Before  | 16 $\pm$ 3                                | 89 $\pm$ 11                          | 286 $\pm$ 63              | 166 $\pm$ 38             | 132 $\pm$ 32             |
|           |           | After   | 9.6 $\pm$ 2.2 <sup>b</sup>                | 29 $\pm$ 9 <sup>b</sup>              | 108 $\pm$ 23 <sup>b</sup> | 86 $\pm$ 22 <sup>b</sup> | 60 $\pm$ 12 <sup>b</sup> |
| Operation | 26        | Before  | 15.3 $\pm$ 3.1                            | 87 $\pm$ 10                          | 263 $\pm$ 54              | 156 $\pm$ 36             | 130 $\pm$ 30             |
|           |           | After   | 9.5 $\pm$ 2.1 <sup>d</sup>                | 27 $\pm$ 8 <sup>d</sup>              | 98 $\pm$ 25 <sup>d</sup>  | 87 $\pm$ 22 <sup>d</sup> | 57 $\pm$ 11 <sup>d</sup> |

<sup>b</sup> $P$ <0.01 vs markers before ENBD, <sup>d</sup> $P$ <0.01 vs markers before operation.

**Table 2** Therapeutic effects of two groups

| Group     | Cases (n) | Remission time of abdominal pain (d) | Complication (cases) | Average length of hospital stay (d) | Average cost (Yuan) |
|-----------|-----------|--------------------------------------|----------------------|-------------------------------------|---------------------|
| ENBD      | 58        | 1                                    | 13                   | 9                                   | 6 503               |
| Operation | 26        | 6 <sup>b</sup>                       | 10                   | 20 <sup>b</sup>                     | 16 300 <sup>b</sup> |

<sup>b</sup> $P$ <0.01 vs ENBD group.

### Observing parameters

The following parameters were measured before and one week after treatment. (1) Changes of the average diameter of common bile ducts, serum total bilirubin, ALP,  $\gamma$ -GT and ALT; (2) Complications, average length of hospital stay and the costs; (3) *Clonorchiasis sinensis* metacercaria in feces in follow-up patients.

### Statistical analysis

All data were analysed by  $t$  test, and the significant level was set at  $P$ <0.05.

## RESULTS

Therapeutic effects are shown in Tables 1 and 2. (1) ENBD group: Jaundice decreased in 72 h and disappeared in 3 wk. The average remission time of abdominal pain was 1 d after ENBD. Nineteen cases with fever returned to normal temperature 48 h after drainage. The dead polyp could be seen discharged from nasobiliary drainage 12 h after oral praziquantel. Peak time of dead polyp discharging was within 24-48 h after oral praziquantel and there was no dead polyp on the fifth day. (2) Operation group: The mean remission time of abdominal pain was 6 d after operation. Jaundice and fever began to decrease 2 d after operation. The dead polyp could be seen discharged from T-tube 12 h after oral praziquantel.

There were 8 cases with transient hyperamylasemia in ENBD group, who were cured in 48 h by fasting, anti-acid and anti-inflammation therapy. Two cases with bile duct retrograde infection after sphincterotomy accompanied with transient fever and chill were cured by anti-inflammation therapy. In all 58 cases, there was no case of bleeding and perforation, but 3 cases developed recurrent disease in 1-2 years and needed therapy again. In operation group, there were 8 cases with gallstone in common bile duct or cholangitis after operation, and 2 cases with intestinal adhesion.

*Clonorchiasis sinensis* metacercaria was found in feces of all the patients of the two groups 3, 6, 12, 18 and 24 mo after ENBD or operation. After oral praziquantel again, no *Clonorchiasis sinensis* metacercaria was found in feces.

## DISCUSSION

*Clonorchiasis sinensis* is an amphixenosis parasitic disease threatening people's health. The average infectious rate was 21.1% in Pearl River Delta region, and up to 88.6% in certain

areas. Oral praziquantel is the first-line therapy drug; its effectiveness can be 98.8%<sup>[3-5]</sup>. When *Clonorchiasis sinensis* infection is accompanied with obstructive jaundice<sup>[6,7]</sup>, obstruction remission and bile drainage should be the most important treatment target. The traditional method of obstruction remission is operation, but operation has some shortcomings, such as big trauma, high costs and recurrence. With the development of endoscopic intervention, the therapy of *Clonorchiasis sinensis* with endoscopic bile duct drainage has bright prospect<sup>[8]</sup>.

Our results showed that oral praziquantel after endoscopic nasobiliary drainage was a safe and effective way for the treatment of *Clonorchiasis sinensis* accompanied with obstructive jaundice. The two methods had equal effects (as shown in Tables 1 and 2), and no significant difference with regard to the remission time of jaundice and average diameter of common bile duct. However, endoscopic nasobiliary drainage did have some advantages, such as rapid remission of fever and abdominal pain, little trauma, rapid recovery, fewer complications, less length of hospital stay and less cost.

Sphincterotomy is required for patients with inflammatory papillary stenosis. Drainage is helpful for decreasing the restenosis after operation. Sphincterotomy is indicated in the following situations: Papilla opening is very small, stiff, and has no bile flow; it is difficult to inject contrast; contrast shows that inferior part of common bile duct is obviously narrow.

Generally, nasobiliary drainage should last 4-7 d and the bile duct should be washed by 5 g/L metronidazol 1-2 times daily. Once the drainage tube is out of place, it is not necessary to re-put drainage if there is no symptom of increasing stenosis, jaundice or fever. The causes of drainage dislocation included: Anterior extremity of nasobiliary drainage had no bents; the papilla opening was too big during sphincterotomy; some patients would pull out the nasobiliary drainage because of irritation and nausea; some patients had too much hiccupping and vomiting. Doctors should make more explanations to get patients' cooperation.

The main complication of endoscopic therapy was transient hyperamylasemia, which was associated with repeated pancreatic duct visualization during contrast imaging. This complication could be relieved by fasting, antacid and anti-inflammation therapy for 48 h. Once there was pancreatitis, the therapy was initiated for acute pancreatitis. In patients with moderate jaundice and good general condition, oral praziquantel could be taken 8 h after endoscopic drainage. Patients with

severe jaundice and severe impairment of hepatic function, should receive therapy to improve and protect hepatic function, and take oral praziquantel 2-3 d after drainage to decrease the damage to liver caused by the drugs.

On the whole, both ENBD and traditional operation are effective for the treatment of *Clonorchiasis sinensis* infection complicated with obstructive jaundice. However, ENBD has some advantages, such as rapid remission of fever and abdominal pain, little trauma, rapid recovery, fewer complications, less length of hospital stay and less cost.

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