INVITED LECTURES

001

DIFFERENTIAL DIAGNOSIS OF JAUNDICE

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Introduction

Jaundice (icterus) is a yellow discoloration of the tissues best perceptible on the skin, mucous, membrane and in the whites of the eyes. It is caused by excessive quantities of bile pigment bilirubin in the blood. Bilirubin is the end product of haem, the major part coming from haemoglobin: senescent erythrocytes, maturation or destruction of newly formed erythrocells, hematomas or intravascular haemolysis. Only about 15–20 % are derivealsod from other haemo-containing proteins, for example, cytochrome P450, or others. Approximately 300 mg of bilirubin is formed daily, largely in the reticulo-endothelial cells of the spleen, the bone marrow, and liver. The normal level of the total bilirubin in serum is 3.4 to 17.1 μmol/l (both children and adults) and the level of the conjugated bilirubin is 0 to 3.4 μmol/l. Jaundice is unambiguously perceptible when the level of bilirubin in serum is higher than 40–50 μmol/l. There are other causes of yellow discoloration of the tissues in addition to bilirubin, for example excessive carotene from carrots. We talk about "pseudoicterus – false jaundice". Typical for this is no discoloration of the eye whites. From a clinical viewpoint we know of three forms of jaundice. Pre-hepatic form. The main cause of this is haemolytic anaemia. The second is the hepatic form whose etiology is usually acute hepatitis or chronic hepatitis, including cirrhosis of heterogeneous etiology. The third form is post-hepatic jaundice. Its etiology is almost always gallstones or malignancy. It is necessary, speaking about jaundice, to mention the term cholestasis. We define this as the state when the normal quantity of bile does not reach the duodenum. It is usually accompanied by jaundice, but no less frequent is unicteric cholestasis, with only laboratory signs of this syndrome. Its etiology can be intrahepatic or extrahepatic. It is very important to differentiate between these two forms of cholestatis for subsequent therapy and this is one of the most difficult differential diagnostic procedures[1, 2, 10, 13, 15].

Formation and metabolism of bilirubin

Metabolism of haem

Haem (ferroprotoporphyrin IX) is a ring of four tetrapyrroles connected by methene bridges. The ring is opened in a reaction catalyzed by microsomal haem oxygenase. High levels of this enzyme activity are present in cells of the spleen, hepatocytes, Kupffer cells and others. The immediate product of haem oxygenase-mediated ring opening is the green pigment biliverdin. This is reduced by biliverdin reductase to bilirubin, which in its unconjugated form is only sparingly soluble in water.[13, 15]

Conjugation of bilirubin

Bilirubin is carried in the circulation to plasma albumin. Binding to albumin prevents precipitation and deposition of bilirubin in tissues and facilitates its reaching the organ elimination, the liver. The albumin – bilirubin complex entering the liver through the portal circulation passes through the fenestrated sinusoids to the space of Disse and through the basolateral membrane to hepatocytes. But, before entering hepatocytes, the albumin – bilirubin complex disassociates and only bilirubin comes to hepatocytes. Metabolism of bilirubin is accomplished in hepatocytes by binding to a group of cytosolic proteins, glutathione-S-transferase, also termed ligandin or Y-protein. Conjugation of bilirubin is done in the endoplasmic reticulum and is catalyzed by bilirubin – UDP – glucuronosyltransferase, forming two forms of conjugated bilirubin: monoglucuronide – bilirubin and diglucuronide – bilirubin. In 1916 van den Bergh and Muller found that one species of serum bilirubin reacts with sulfanilic acid diazoreagent within minutes of "direct reaction fraction", whereas the other reacts rapidly only when acceleration substances, for example methanol, are present. This is called "indirect reacting fraction". Later it was understood that indirect – reacting bilirubin represents unconjugated bilirubin, and direct – reacting bilirubin corresponded to conjugated bilirubin. The discoverer of this phenomenon was, among others, the Czech scientist E. Talafant (Brno), who described this in 1956. The conjugated bilirubin is transported through the biliary membrane to the bile canaliculus and shared by other organic anionts, but not the bile salt[13, 15, 16].

Bilirubin in the gastrointestinal tract

Conjugated bilirubin after reaching the intestine is deconjugated by the intestinal bacteria and degraded into a series of urobilinogens (urobilinogen, stercobilinogen, mesobilinogen). About 30 % of this is absorbed in the intestine into the portal blood and re – excreted in the bile and to a lesser extent in the urine. But, urobilinogens are not glucuronidated, because they are soluble in water. The higher level of urobillinogens, for example in the haemolysis, extends excretion of urobilinogens in the urine. On the other hand, the absence of urobilonogens in stool (acholic stool) and urine indicates the complete obstruction of bile ducts. About 70 % of urobilinogens passing through the small and large intestine, are oxidised to urobilins (urobilin, stercobilin, mesobilin), causing the brown coloration of stool.[13, 15]

Clinical classification of jaundice

There are many different classifications of jaundice more precisely classifications of hyperbilirubinemia. It is necessary at this moment to say that there are no pathological situations for which a lower level of bilirubin in serum will be characterised. One divides jaundice from the aspect of conjugation into two types: jaundice with preponderantly unconjugated hyperbilirubinemia. Typical examples are haemolytic anemias or Gilbert's syndrome. Jaundice with preponderantly conjugated hyperbilirubinemia. A typical example of this is cholestatic jaundice. The best classification, from the clinical aspect, is to divide jaundice into three groups. Pre-hepatic, hepatic and post-hepatic jaundice[2, 4, 9, 13, 14, 15].

Hereditary nonhemolytic benign hyperbilirubinemia

This is a special group of hyperbilirubinemia with hereditary etiology and a good prognosis, except for Crigler – Najjar's syndrome, which fortunately is very, very rare. The main representative of this group is Gilbert's syndrome, with an incidence of about 5 % and with benign prognosis. Its characteristic sign is a stable unconjugated hyperbilirubinemia, but not higher than about 30–40 μmol/l. The level of unconjugated bilirubin serum rises only at certain conditions and jaundice can be identified. These conditions are physical or emotional tiredness, infectious illness, fasting, and others. On the other hand some drugs reduce the level of bilirubin, for example phenobarbital.

These characteristics can be used in a diagnostic test of Gilbert's syndrome. The second type of unconjugated hyperbilirubinemia, as already mentioned, is the Crigler – Najjar's syndrome. Dubin – Johnson's syndrome and Rotor's syndrome belong to a group of conjugated hyperbiliruninemia with hereditary etiology and also benign prognosis. Their incidence is low[1, 2, 3, 9, 13, 15, 17].

Pre – hepatic jaundice

The main cause of hepatic jaundice is haemolysis. Jaundice has a goldyellow tinge. Elevated plasma levels of bilirubin are of the unconjugated type. Urobilinogen is detectable in urine, but bilirubin is absent. The stool has a dark brown tinge – hypercholic stool. The other laboratory liver tests are normal and it is necessary to search for causes of haemolysis, especially for hemolytic anaemia (5).

The main laboratory evaluation of haemolysis:

Hematologic: routine blood film, reticulocyte count, bone marrow examination, to search for the morphology abnormalities of red blood cells: spherocytes, target cells, sickled cells, acanthocytes, agglutinated cells, Heinz bodies.

Plasma or serum: bilirubin, haptoglobin, plasma hemoglobin, lactate dehydrogenase, Coombs test, iron.

Urine: bilirubin, hemosiderin, hemoglobin

Classification of hemolytic anaemia:

Hereditary: Abnormalities of RBC interior: enzyme defects, hemoglobinopathies RBC membrane abnormalities: hereditary spherocytosis etc.

Acquired: RBC membrane abnormalities: poraxysmal nocturnal hemoglobinuria, spur cell anaemia.
Extrinsic factors: hypersplenism, immune hemolysis, microangiophatic hemolysis, infections, toxins, etc.

Hepatic jaundice

Hemoglobin catabolism is normal, but the intrahepatic transport of bilirubin and/or its conjugation is disturbed. This causes hepatocellular damage, but certain cholestatic components also play a role in the pathogenesis of jaundice. Higher serum levels of both types of bilirubin are present. Stool is sometimes of normal colour, at other times, with the higher grade of hepatocellular damage, it is light (hypocholic stool) due to a low concentration of urobilinogen. Urobilinogen is presented regularly in the urine, but bilirubin is present only in serious cases. Jaundice can present with a ruby tinge. Hyperbilirubinemia in connection with hepatocellular damage is a sign of liver insufficiency or failure. The physical examination shows, without jaundice, hepatosplenomegaly, spider naevus, signs of bleeding into the skin – petechiae, suffusions, ecchymoses, hematoma, signs of portal hypertension – ascites, caput medusae, bleeding into the gastrointestinal tract, signs of hepatic encephalopathy – from disturbance of mental function through sleepiness, apathy, to coma, flapping tremor, etc.[1, 2, 6–8, 10, 14]

The main laboratory or other evaluations:

Test of integrity of hepatocytes: alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyltransferase (GGT)
Markers of synthetic function of liver: albumin, cholesterol, prothrombin time, cholinesterase, fibrinogen, antithrombin III, ammonia etc.

Evidence of etiology:

- virological evaluation – markers of virus hepatitis A,B,C,D,E,G,
- immunological evaluation – antinuclear antibodies (ANA), antimitochondrial antibodies (AMA), antibodies against soluble liver antigens (SLA), smooth muscle antibodies (SMA), liver-kidney-microsomal antibodies against cytochrome P450 IID6 (LKM-I), immunoglobulins, etc.,
- markers of metabolic and toxic disorders – iron, ferritin, transferrin, copper, caeruloplasmin, porphyrins, markers of diabetes mellitus, markers of alcohol abuse, evaluation of lipid spectrum, etc.
- ultrasonography
- liver biopsy

Etiology of hepatic jaundice:

Acute hepatitis: acute viral hepatitis: A, B,C, D, E, G, TT, EBV, CMV,
acute toxic and drug hepatitis: acetaminophen, halotan, ethanol, amanita poisoning, amiodarone, etc,
metabolic disorders: Wilson disease etc.,
cardiovascular failure: constrictive pericarditis, acute myocardial infarction with or without congestive cardiac failure, Budd Chiari syndrome etc.,
pregnancy: idiopathic acute fatty liver of pregnancy, syndrome of haemolysis, abnormal liver function tests, and low platelets (HELP syndrome),
complications after liver transplantation.

Chronic liver disorders:
chronic viral hepatitis: B, C, D, G,
autoimmune hepatitis,
liver fibrosis or cirrhosis of different etiology
primary or secondary tumors of the liver

Post-hepatic jaundice, cholestatic jaundice

Cholestasis is a clinical and biochemical syndrome characterized by pruritus, jaundice and elevation of serum alkaline phosphatase (ALP) and GGT. Hyperbilirubinemia however is not necessary. At first it was believed that only mechanical obstruction of the biliary ducts could be the cause of cholestasis. Virchow thought that jaundice in viral hepatitis resulted from obstruction of the ampulla of Vater by a mucous plug. Later it was documented that even disorders on the biliary membrane can cause cholestasis, the best documented examples of some hepatocellular damage being viral hepatitis with cholestatic course, pregnancy, drug liver disorders etc. At present, cholestasis is defined as the state when bile does not reach the duodenum[3–5, 7, 9, 10–12, 14]. Cholestasis is divided according to pathological processes into intrahepatic and extrahepatic cholestasis, from the presence of hyperbilirubinemia into icteric and anicteric forms, and from the presence of symptoms into symptomatic and asymptomatic cholestasis.

Approach to patients with cholestasis:

Routine investigation: clinical evaluation, full blood count, ESR, urea and electrolytes, bilirubin, albumin, and globulin, ALT, AST, ALP, GGT, prothrombin time, chest radiograph, abdominal ultrasound (USG)

USG finding favours intrahepatic cause (normal – size ducts, or splenomegaly, or abnormal liver rexture):
exposure to hepatitis, drug abuse, alcohol abuse, stigmata of chronic liver disease, splenomegaly

USG finding favours extrahepatic cause (dilated intrahepatic, or extrahepatic bile ducts, or pancreatic mass):
abdominal pain, rigors, severe weight loss,

previous biliary surgery, palpable gallbladder or pancreatic mass.
Evaluation: ERCP, PTC, CT, IMR. ESG,

Classification of intrahepatic cholestasis:
- Hepatitis: viral (A, B, C, Epstein-Barr, CMV), autoimmune, alcoholic
- Drugs and hormones
- Disease of intrahepatic bile ducts: primary biliary cirrhosis, intrahepatic sclerosing cholangitis, graft-versus-host disease, sarcoidosis,
- Liver infiltration / storage disorder: lymphoma, amyloidosis, Wilson's disease, haemochromatosis, protoporphyria
- Systemic infection
- Total parenteral nutrition
- Postoperative intrahepatic cholestasis
- Cholestasis of pregnancy
- Benign recurrent intrahepatic cholestasis

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002

PROBIOTIC THERAPY OF INFLAMMATORY BOWEL DISEASE (IBD)

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IBD arises in genetically susceptible individuals owing to a breakdown in the regulation of response of the mucosal immune system (MIS) to antigenic stimuli from the intestinal contents. These stimuli have not been identified on the molecular level, but there is growing evidence that the mucosal microflora plays a pivotal role in the process. This micro-flora is present in high concentrations even in parts of the digestive tube unaffected by the inflammatory process.
At present most current drug therapy of IBD is oriented to blockade or suppression of the host immunoinflammatory response. However, the ultimate therapeutic goal is prevention of intestinal inflammation. Such approach requires elimination of dominant antigens chronically stimulating the MIS and blockade of the mucosal immune response to these stimuli. Both processes may be favourably affected by the use of probiotics.
Probiotics are live microorganisms of human origin that may influence human health and prevent or ameliorate certain diseases. The effect of probiotics is closely connected with prebiotics, i.e. such food components that cannot be digested by any enzyme system of the small intestine and serve as microbial substrates in the colon (e.g. oligofructans, fiber). Probiotics and prebiotics together modulate a composition of intestinal flora in favour of the host. The safety of probiotic therapy requires that microorganisms fulfil multiple criteria including detailed typing, no pathogenic properties, human origin, application to the living organism, resistance to digestive secretions, adherence to colonocytes, colonization of the gut, beneficial effect on health, and safety. Probiotics used for therapeutic purposes include various strains of Lactobacilli, Bifidobacteria, non-pathogenic Escherichia coli, Streptococcus salivarius, and the yeast Saccharomyces boulardii.
Probiotics have been tested in experimental enterocolitis, idiopathic proctocolitis (IPC), Crohn's disease (CD) and pouchitis. In IPC and CD clinical studies have shown the equivalent efficacy of probiotics and 5-aminosalicylic acid (5-ASA) in maintenance therapy of the disease as well as the advantage of combined use of probiotics and 5-ASA in active disease. In pouchitis probiotics have proven effective both as part of the therapeutic regimen in acute disease and in the prevention of relapse in chronic disease. Probiotics are nonpathogenic commensal microorganisms. Safety and minimal adverse effects represent the great advantage of this new therapeutic approach.

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003

TIMING OF SURGERY IN PATIENTS WITH OBSTRUCTIVE JAUNDICE

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Key words: Obstructive jaundice / Pancreatoduodenectomy / Bile duct decompression / Biliary stent

Abstract

The proposed benefits of the preoperative bile duct decompression include lower incidence of infection, improved liver function, decreased perioperative bleeding, decreased postoperative sepsis and renal failure. However, several authors have failed to show any effect of preoperative biliary drainage in patients with biliary obstruction undergoing pancreatoduodenectomy or other major surgical procedures in this area, whereas others have even reported an increased morbidity when stent was used. Routine use of preoperative instrumental release of biliary obstruction in patients who are candidates for major surgery of pancreas or biliary tract does not influence overall morbidity nor mortality and it still remains controversial.

Introduction

The value of preoperative decompression of an obstructed bile duct has been discussed over the past decades. Today decompression of the obstructed bile duct becomes easier and safer due to widespread use of endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC). The proposed benefits of the preoperative bile duct decompression include a lower incidence of infection, improved liver function, decreased perioperative bleeding, postoperative sepsis, renal failure and better healing. However, despite these proposed benefits of the preoperative treatment of jaundice, most of the prospective and retrospective reports of biliary duct decompression do not demonstrate an advantage of this procedure. The majority of these studies show no difference in early or later outcome between patients with or without preoperative biliary drainage.

Discussion

Biliary obstruction causes disturbances in liver physiology. In addition several experimental studies have shown that obstructive jaundice leads to: alteration in glycogen metabolism, protein turnover, impaired mitochondrial and hepatic reticuloendothelial function, decreased cell-mediated immunity, high levels of circulating endotoxins, and decreased synthesis of several haemostatic factors. Patients with obstructive jaundice are at risk of postoperative renal failure, intraoperative and postoperative haemorrhage, and deterioration in liver function.

It has been shown that patients with liver disease and hyperbilirubinaemia have abnormal renal structure and function, abnormal circulatory haemostasis, and deterioration in the gastrointestinal barrier to infection. All these aforementioned factors may contribute to the postoperative risk of renal failure. To prevent this postoperative renal failure and other disturbances in patients, the proposed principles of preoperative treatment include the treatment of sepsis, avoidance of nephrotoxic drugs, treatment of renal impairment, and the correction of hypovolaemia, hypoallbuminaemia, hyponatremia and anaemia. Preoperative renal failure will require correction of the fluid balance, the administration of antibiotics, and dialysis, if necessary.

Obstructive jaundice also compromises the immune function. Predisposing factors include impaired phagocytic function, depressed cellular immunity, an exaggerated cytokine response, increased production of reactive agents, decreased endotoxin neutralisation and an impaired gut barrier function[1]. Modulation of the impaired immune response has been tried, however results of the restoration of immune functions have so far not been persuasive[1].

Several authors have therefore proposed relieving of biliary obstruction preoperatively in order to correct the alterations induced by jaundice and to reduce the perioperative mortality and morbidity[2, 3].

In recent years patients with obstructive jaundice are referred to endoscopists who not only diagnose the obstruction but also try to treat it with a stent insertion. If this is not possible, then the biliary decompression is usually achieved radiologically via a PTC drain. Surgeons examining patients with biliary stents then have no other choice but to place them into the therapy as the stent has already been inserted. Routine practice is then waiting for normalisation or improvement of liver enzymes and only then these patients are admitted to surgery.

However, biliary endoprostheses also have local effects on the bile ducts, thus a subsequent bacterial contamination of the bile should be considered. Karsten and colleagues in an experimental study in dogs induced inflammatory changes in the bile ducts by stent insertion and studied the reversibility of these changes after stent removal[4]. They focused particularly on the consequences during the period of preoperative stenting for subsequent operation of the biliary tract and the effect of stenting on the histologic factors of the liver[4]. Four weeks of stenting of a normal or obstructed common bile duct resulted in fibrosed bile ducts, showing severe chronic inflammation. All bile cultures grew fecal bacteria. Two months after stent removal, the inflammation was still present, however, it was less severe. Stenting and subsequent surgical treatment resulted in a higher incidence of postoperative complications compared to the control group. Hepatic histological factors were not markedly changed after transpapillary endoprosthesis placement[4].

Martignoni et al. retrospectively analysed a consecutive series of 257 patients undergoing pancreatoduodenectomy[5]. Ninety-nine patients (38 %) underwent preoperative biliary drainage for a median time of 10 days prior to resection. The postoperative morbidity was 47 %, the re-operation rate was 4.3 %, and mortality was 2.3 %. There was no difference in total morbidity, infectious complications, re-operation rate, mortality, or long-term survival between patients with or without preoperative biliary drainage. Thus was concluded that preoperative biliary instrumentation and biliary drainage do not affect the early or late outcome in patients undergoing pancreatoduodenectomy[5].

Many published studies characterise the effects of preoperative biliary drainage in patients with resectable as well as unresectable malignant obstruction of the common bile duct. The majority of these studies are retrospective and had failed to show any benefit of preoperative biliary drainage[2, 6–13]. Moreover, three prospective randomised trials using preoperative external transhepatic biliary drainage failed to show any effect on the surgical outcome[14–16], whereas randomised studies examining endoscopic internal biliary drainage have reported contradictory results. Several reports have shown that especially percutaneous transhepatic biliary drainage carries its own morbidity[15–16]. Therefore, the indication for preoperative release of biliary obstruction remains controversial.

Several studies refer to another possible reason why the preoperative biliary drainage failed to help patients with severe jaundice, which appears to be its insufficient duration: between 2 to 3 weeks. Experimental data in animals with bile duct ligation showed that alterations in liver function normalised within 5 days, other cellular

pathways such as beta-oxidation and other mitochondrial functions needed 2 to 6 weeks to normalise.
In patients with pancreatic or ampullary mass and obstructive jaundice, routine preoperative biliary drainage is not warranted. Patients do not benefit from the preoperative internal biliary stenting, with an exception of patients with long-lasting biliary obstruction and hepatic alteration. These patients and also patients, who cannot undergo surgery within 2 to 3 weeks, may benefit from temporary biliary drainage, as this can resolve clinical symptoms or prevent further deterioration of liver function. However, these patients may be more prone to infectious complications.

Conclusion

Routine use of biliary instrumentation in patients who are candidates for the major surgery of pancreas or biliary tract does not influence overall morbidity or mortality. In conclusion in the era of magnetic resonance cholangiography the indication for preoperative release of biliary obstruction still remains controversial. Several authors have failed to show any effect of preoperative biliary drainage in patients with biliary obstruction undergoing pancreatoduodenectomy or other surgical procedures in this area, whereas others have even reported an increased morbidity when stent was used.

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004

HEPATIC COMPLICATIONS OF SURGERY

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Patients with cirrhosis of the liver have a reduced life expectancy. Anesthesia and surgery have been associated with clinical decompensation in cirrhotic patients. It has been estimated that 10 % of cirrhotics undergo at least one operative procedure during the final 2 y of their lives. Surgery in the patient with liver disease, notably open abdominal surgery, carries a high risk of morbidity and mortality. Child-Pugh's classification remains the standard for preoperative risk assessment. The mortality rate of open abdominal surgery lies between 3–10 % for cirrhotics grade A, 10–30 % for grade B and 50–80 % for grade C. Prothrombin time alone is closely correlated with the outcome: mortality of 1 % has been reported for open cholecystectomy in cirrhotics with normal prothrombin time, 9 % in patiens with PT prolongation up to 2.5 sec and 83 % in patients with PT prolonged by more than 2.5 sec. Several other factors influencing the postoperative outcome have been identified including malnutrition, hyperbilirubinemia, hepatic encephalopathy, and ultrasonographic signs of portal hypertension such as dilated portal vein or increased splenic size and others. In a Mayo Clinic study of 733 surgical patients with liver cirrhosis the perioperative mortality rate (within 30 days of surgery) was 11.6 % and the perioperative complication rate was 30.1 %. Postoperative pneumonia was the most frequent complication. Multivariate factors that were associated with perioperative complications and mortality included male gender, a high Child-Pugh score, the presence of ascites, a diagnosis of cirrhosis other than primary biliary cirrhosis (especially cryptogenic cirrhosis), an elevated creatinine concentration, and others.
In patients with liver cirrhosis, gastroduodenal ulcer disease and its complications are common. In a study of 69 patients with liver cirrhosis undergoing surgery for gastroduodenal ulcer disease, 90 % of patients required emergency surgery for bleeding ulcer or perforation. Mortality was 29 % for elective patients, 35 % for patients with perforation and 64 % for patients with bleeding. Overall mortality of 69 patients was 54 %. Only 15 of 69 patients (22 %) had an uncomplicated postoperative course. Postoperative bleeding, septic complications, and renal failure were the most frequent postoperative complications. Bleeding and multiple organ failure were the leading cause of death in 70 % of patients.
In a cohort of patients with chronic liver failure undergoing nonhepatic surgery, thirty-day mortality was 28 % and an international normalized ratio greater than 1.6 and encephalopathy were associated with a greater than 10- and 35-fold increased mortality risk, respectively. Child classification and Pugh score failed to predict 30-day mortality.
In another study, a mortality of 21 % was reported in cirrhotic patients with major abdominal surgical interventions. Suture-line insufficiency, peritonitis, sepsis and other inflammatory processes turned out to be the most common complications. Statistical analysis showed that

the Child criteria, prothrombin level and white blood cell count were useful prognostic factors.

In a well-designed study, 92 patients diagnosed with cirrhosis required either an emergent or elective abdominal operation. Coagulopathy developed in 24 patients (27 %) and sepsis in 15 (16 %). The mortality rate after emergent operations was 50 %, compared to 18 % for elective cases (p = 0.001). Other factors that predicted mortality included the presence of ascites (p = 0.006), encephalopathy (p = 0.002), and elevated prothrombin time (p = 0.021). The mortality in Child's class A patients was 10 %, compared to 30 % in class B and 82 % in class C patients.

The impact of emergent procedures on mortality has been corroborated by other authors. In a study of 77 cirrhosis patiens who underwent abdominal surgery, the 30-day mortality rate was 18 percent. Emergent operations were associated with a mortality rate of 32 percent compared with 8 percent after elective procedures (p < 0.05). Extensive complications occurred in 28 percent of patients (14 percent after elective operative treatment and 49 percent after emergent procedures). The mortality rate was greatest after gastric procedures (38 percent). Other factors of statistical significance (p < 0.05) associated with poor postoperative outcome included cachexia, preoperative transfusion of fresh frozen plasma, and intraoperative platelet transfusion. Surprisingly, operative blood loss, presence of ascites, and operative time were not associated with increased complications or death. The authors conclude that elective, nonshunt abdominal operations can be performed with acceptable morbidity and mortality rates in selected patients with cirrhosis.

Biliary surgery in cirrhotic patients carries a considerable risk. Of 39 cirrhotic patients operated on the biliary tract eight patients died (21 %), and major complications were found in 12 surviving patients (35 %). Local and systemic sepsis was the major contributor, accounting for all of the deaths and 17 of the 22 (77 %) complications among survivors. Choledochotomy was done in ten patients; three of them died (30 %) and nine major complications occurred in the remaining five. Preoperative risk factors found to be predictive of this high morbidity and mortality were ascites (50 % mortality, 50 % morbidity), prolonged prothrombin time (29 % mortality, 38 % morbidity), and a serum albumin level of less than 3.5 g/l (33 % mortality, 40 % morbidity). The presence of other major systemic disease was not significantly different between survivors and nonsurvivors. In 12 patients with no ascites and normal preoperative serum chemistry values, no deaths and only one minor complication occurred. In the authors' view, operative therapy in these patients should be reserved for the complications of the biliary tract.

In a study of 135 patients with liver cirrhosis undergoing nonhepatic procedures and 86 matched controls, the patients with cirrhosis showed higher blood transfusion requirements, extended hospital stay, and higher number of complications than the controls. The mortality rate was 16.3 % in cirrhotics and 3.5 % in controls. By univariate analysis, the need for transfusions, prothrombin time, and Child-Pugh score were significantly associated with postoperative liver decompensation, whereas duration of surgery, prothrombin time, Child-Pugh score, cirrhosis-related complications, and general complications were significantly associated with mortality. In the multivariate analysis, Child-Pugh score, duration of surgery, and postoperative general complications were independent predictors of mortality. Laparoscopic cholecystectomy in patients with Child's class A and B cirrhosis was found to be reasonably safe and showed no increase in morbidity or mortality or worsening of outcome.

Another major surgical challenge is liver resection in cirrhotic patients with hepatocellular carcinoma (HCC). In a selected group of 108 Child-Pugh A cirrhotic patients undergoing liver resection of HCC, the overall incidences of in-hospital deaths and postoperative complications were 8.3 % and 48.1 %, respectively. By univariate analysis, the preoperative serum alanine transferase (ALT) level (p = 0.001) and intraoperative transfusions (p = 0.01) were significantly associated with in-hospital death. However, only the serum ALT concentration was an independent risk factor. In-hospital mortality rates in patients whose serum ALT was below 2N (twofold the upper limit of the normal value), between 2N and 4N, and more than 4N were 3.9 %, 13.0 %, and 37.5 %, respectively. An ALT level greater than 2N was predominantly observed in patients with a hepatitis C virus infection and significantly associated with histologic features of superimposed active hepatitis. Patients with an ALT level greater than 2N experienced an increased incidence of postoperative ascites (58 % versus 32 %, p < 0.01), kidney failure (16 % versus 0 %, p = 0.0003), and upper gastrointestinal bleeding (6.4 % versus 0 %, p = 0.02). The authors recommend that cirrhotic patients with ALT > 2N undergo only a limited resection; if a larger resection is required, those patients should be considered for nonsurgical therapy or liver transplantation.

The importance of evaluating ALT activity is further stressed by the fact that patients incubating viral hepatitis have extraordinarily high morbidity and mortality when subjected to the stress of anesthesia and surgery.

Also in cardiac surgery, mortality rate depends on severity of liver disease. The overall perioperative mortality rate in a group of patients with liver cirrhosis was 31 %. In patients with Child class B cirrhosis, the mortality rate was 80 %. No patient with Child class A cirrhosis died. Deaths were related to gastrointestinal and septic complications, and not to cardiovascular failure. In the authors' view patients with minimal clinical evidence of cirrhosis can tolerate cardiopulmonary bypass and cardiac surgical procedures, whereas those with more advanced liver disease should not be offered operation.

In patients requiring major otolaryngology procedures, a history of hepatitis and prolonged anesthesia time were found as the only independent predictors of medical complications.

Also transurethral resection of the prostate in patients with liver cirrhosis carries a risk of about three-times increased mortality in comparison with patients with a healthy liver.

In a Danish study, hysterectomy in women with liver cirrhosis was associated with a 11-fold increased risk of death within the first 30 days after discharge.

Prolonged Q-T interval predicts severe arrhythmias and sudden death, and has been shown to occur in alcoholic liver disease and cirrhotic patiens. Ninety-four patients with cirrhosis without overt heart disease and 37 control subjects with mild chronic active hepatitis were studied. Q-Tc was longer in patients with cirrhosis than in controls (440.3 +/– 3.2 vs. 393.6 +/– 3.7 ms; P < 0.001) and prolonged (> 440 ms) in 44 patients (46.8 %) and 2 controls (5.4 %; P < 0.001). Q-Tc length was not influenced by the etiology of cirrhosis and correlated with Child-Pugh score (r = 0.53; P < 0.001), liver tests such as prothrombin activity, and serum concentrations of albumin and bilirubin, plasma bile salts, and plasma norepinephrine. Multivariate analysis showed that only Child-Pugh score and plasma norepinephrine were independently correlated with Q-Tc duration. Over a median follow-up period of 19 months, patients with Q-Tc longer than 440 ms had a significantly lower survival rate than those with normal Q-Tc.

To conclude, sugical procedures under general anesthesia in cirrhotics carry significant morbidity and mortality risks. These can be diminished by intensive preoperative care, with minimizing intraoperative blood loss, avoiding emergent procedures as far as possible and using laparoscopy and other modern techniques.

005

TOPICAL STEROIDS

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Corticosteroids have been successfully used in treatment of the idiopathic bowel disease (IBD) for more than fifty years[1]. They are used for their anti-inflammatory and immunomodulative effects based on inhibition of the inflammatory cytokines, migration of granulocytes, inhibition of macrophages and mastocytes, and suppression of lymphocytes. Steroids reduce activity of phospholipase A_2, which reduces the synthesis of prostaglandins and leukotriens. The most often used drugs with systemic effect in IBD therapy are hydrocortisone, prednisolone, methylprednisolone, and triamcinolone.

Glucocorticoids are used in treatment of Crohn's disease (CD) as well as ulcerative colitis (UC). In patients with high inflammatory activity, glucocorticoids are mostly administered parenterally in a dose matching 1–1.5 mg of prednisolone per kilogram of patient's weight. In inflammations of low or medium activity, the medicine is administered locally when aboral colon is affected, or perorally when other parts of small intestine or colon are affected. The dose matches 0.5 mg of prednisolone per kilogram of patient's weight. In IBD maintenance therapy, the effectiveness of corticoids was not registered regardless of administration.

However, some side effects have been observed even in the case of local administration of these drugs and therefore there is a tendency to develop and implement new drugs of the same efficiency that would have no or minimum negative side effects.

Possible Negative Side Effects in Short-term Impulse Corticotherapy

- ventricular arrhythmia and manifestations of cardiac insufficiency
- disruptions of glucose metabolism
- impairment of GIT mucosa
- thromboembolic disease
- flush

Possible Negative Side Effects of Long-term Corticotherapy

- suppression of immune reactions – reduction of resistance to bacterial, viral, mycotic and parasitic infections
- diabetogenic effect – manifestation or decompensation of diabetes mellitus
- influence on the CNS – insomnia, disorders of motor system, vertigo, cephalea, psychotic disorders
- gastrointestinal – exacerbation of ulcerous disease of gastroduodenum, induction of acute pancreatitis
- skeletal system – steroid myopathy, osteoporosis
- cardiovascular – hypertension, steroid cardiomyopathy, increased coagulability with thromboembolic disease
- others – dermal, endocrine, metabolic

In the eighties, new corticoids with local effects became available, such as beclomethasone dipropionate, prednisolone sodium metasulfobenzoate and fluticasone propionate. Currently budesonide proves to be the most promising and effective drug in IBD treatment with minimum corticoid side effects and contraindications. However, patients sensitive to the working substance or to its additives cannot use budesonide. Naturally, patients with serious bacterial, mycotic or viral bowel infections must not use it at all.

For treatment of lower or medium stage of UC affecting colon up to the lienal flexure, budesonide is available in a form of rectal enema to be applied locally (Entocort 2 mg enm. tbl. + sol.). It is administered for a period of 3–6 weeks, one enema per day.

Peroral form is indicated for treatment of moderate or medium CD affected ileum, cecum and colon ascendens, in a form of CIR controlled-release gelatinous capsules delivered to the region of ileocecum (Entocort 3 mg cps.), or pH-dependent release tablets (Budenofalk 3 mg tbl.) Treatment starts with 9 mg daily dosage, the period of treatment depends on disease's seriousness and progress. Full therapeutic effect is mostly achieved after 2–4 weeks of treatment, then the treatment should continue for 6–8 weeks with 9 mg daily dosage. Administration of budesonide should not be stopped suddenly, it is recommended to finish the treatment by gradual reducing of the dosage.

Advantages of Topical Corticoids Usage

- prolonged retention and higher concentration in the area of application
- high selectivity to mucosa
- high affinity to corticosteroid receptors
- high metabolic inactivation (90 % of the topical steroid is inactivated during the first pass through liver by conversion into metabolites with minimum biological activity)
- prolonged absorption from the area of application
- dilution in the system circulation
- no mineralocorticoid effects

In the 1990s, many studies observed the effect of topical corticoids, namely budesonide in IBD treatment, both in establishing remission and keeping the maintenance therapy.

For the active left-sided and rectal form of UC, rectal-enema budesonide is successfully used to establish remission. In 1996, Lofberg carried out a large comparative study of perorally administered budesonide (10 mg) and prednisolone (40 mg) in patients with active left-sided or extensive type of UC for a period of nine weeks. Lofberg did not show the importance of the perorally administered budesonide in comparison with prednisolone[2]. After two-month treatment, the clinic, endoscopic and histopathologic findings brought evidence in favor of prednisolone. In the maintenance therapy of UC, the efficiency of corticoid treatment, either topical or systematical, was not evidenced[3].

Perorally administered budesonide has been originally designed for treatment of CD, therefore the majority of studies on this drug was carried out in patients with CD.

In 1994, Greenberg, in a set of 258 patients with active CD in ileocecal region, brought evidence that budesonide in a daily dosage of 9 mg for a period of 8 weeks is very well tolerated and much more effective than placebo or budesonide in lower dosage to establish the remission[4]. In the same year, Rutgeerts carried out a comparative study of budesonide and prednisolone in active CD. In a set of 176 probands, he proved that budesonide as well as prednisolone are effective for establishing remission[5]. In this study, prednisolone remarkably reduced the activity index of CD (CDAI), on the other hand, patients treated by budesonide had much lower occurrence of negative side effects caused by administration of corticoids.

To establish remission in patients with active CD, budesonide (9 mg daily dosage) is much more effective than mesalazine (2 mg daily dosage). This finding was confirmed by the study of Thomsen in 1998: 93 patients used budesonide in a form of CRI capsules and 89 mesalamine in a form of controlled-release tablets[6]. After a period of eight-week treatment, 69 percent of patients treated with budesonide were in remission while in a group with mesalazine, only 45 procent were in remission. The treatment was finished

after 16 weeks and at that time, 62 percent of budesonide treated patients were in remission, while only 36 percent of patients treated with mesalazine were in remission, which is a statistically important variance ($p < 0.001$).
Topical corticoids were tested also in maintenance therapy of CD. Both Greenberg in 1996 and Lofberg in 1999 evidenced that the daily dosage of 6 mg of budesonide used within the maintenance therapy of CD delays the outburst of the disease in patients with medicament-based remission, but this treatment does not meet the criteria for keeping the remission for a period longer than 1 year[7, 8].

Conclusion

1. Since the beginning of the 1990s, topical corticoids are used in IBD treatment. Administered locally or systematically, topical corticoids remarkably reduce the occurrence of negative side effects and their iterative administration does not cause suppression of hypothalamic-pituitary-adrenal axis.
2. In the treatment of active left-sided and rectal form of UC, rectal-enema budesonide is highly effective but has no importance in treatment of extensive active UC or in maintenance therapy of UC, regardless of administration as tablets or enemas.
3. In the treatment of active CD in ileocecal region, the use of 9 mg daily dose of controlled-release tablets of budesonide is much more effective than placebo or mesalazine. To establish remission, budesonide has the same effects as prednisolone. However, the occurrence of negative side effects is remarkably lower in treatment based on topical corticoids. In the maintenance therapy, budesonide is only effective in prolongation of CD relapse.

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006

HIATAL HERNIA = GASTROESOPHAGEAL REFLUX DISEASE?

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Distance between the position of the crural impression and the gastroesophageal junction was recorded and hiatal hernia was diagnosed if the distance was less than 2 cm. Herniation occurred in the three forms: 1. hiatal (axial, sliding) type in which the distal esophagus and portion of the stomach are situated above the diaphragm, 2. paraesophageal type in which the esophagus and gastroesophageal junction retained below the diaphragm and varying portion of the proximal stomach protrudes into the thorax alongside the esophagus, 3. type is a combined sliding and paraesophageal hernia. The cause of hiatal hernia is loosening or laxicity in connective tissue supporting the hiatus and its contents. Hiatal hernia alters the physiology of the gastroesophageal reflux disease by several mechanisms such as disruption of the diaphragmatic sphincter, reduction in lower esophageal sphincter pressure, and impairment of esophageal clearance of acid. Preponderance of patients with gastroesophageal reflux disease has hiatal hernia. But the majority of patients with sliding hiatal hernia are asymptomatic, or the symptoms attributed to a cause-complicated hiatal hernia. Clinically significant symptoms of sliding hiatus hernia are those of gastroesophageal reflux disease. The presence of hiatal hernia was detected most often in the course of barium-contrast radiography. Endoscopy is the first-line diagnostic procedure and most hiatus hernias are now detected this way. Hiatal hernia in the absence of symptoms properly attributed to the hernia necessitates no treatment. The management of hiatus hernia with symptoms of gastroesophageal reflux disease is the treatment for this reflux. Hiatus hernia may or may not be an initiating factor at the inception of reflux disease.

007

INTRAHEPATIC CHOLESTASIS

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Background

Cholestasis is defined as a failure of bile to reach the duodenum in sufficient amounts. Bile secretion is mediated by specific hepatobiliary transport systems in hepatocytes and cholangiocytes for bile salts, other organic anions (bilirubin), phospholipids and electrolytes. Intrahepatic accumulation of biliary constituents results in histopathological features such as bilirubinostasis and cholate stasis, and induction of cholestatic liver enzymes. Accumulation of bilirubin constituents in the systemic circulation results in elevation serum level of bile acids, conjugated bilirubin and jaundice, and cholesterol with formation on xanthomas and xanthelasmas. Pruritus, fatigue and metabolic bone disease represent the three major extrahepatic manifestations of chronic cholestatic liver disease.

Causes and Clinical Spectrum of Cholestasis

Intrahepatic cholestatsis may result either from a functional defect in bile formation at the level of the hepatocyte or from an impairment in bile secretion and flow at the bile duct level.
Clinically, bland (non-inflammatory) versus inflammatory hepatocelllular cholestasis (cholestatic hepatitis) must be distinguished from vanishing bile duct syndromes (VBDS).
Hepatocellular forms of cholestasis usually present as an acute cholestatic jaundice, while jaundice is a rather late feature in the chronic course of VBDS as a primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC) and may rather indicate decompensation. Bland (non-inflammatory) cholestasis is characterized by elevation of serum bilirubin and cholestatic liver enzymes, while inflammatory cholestasis is also accompanied by elevated transaminases. Bland

cholestatis is characterized histologically by purely hepatocellular cholestasis and may result from dose-dependent inhibition of bile secretion by steroid hormones (e.g., estrogens, anabolic steroids, intrahepatic cholestasis in pregnancy, drugs (e.g. tamoxifen, fusidate) and hereditary transport defects (e.g., benign recurrent intrahepatic cholestasis). Induction of proinflammatory cytokins may also produce functional inhibition of hepatocellular bile secretion. Cholestatic hepatitis is characterized histologically by hepatocellular necrosis and lobular/portal inflammation and may be caused by idiosyncratic drug reactions (in particular antibiotics and psychotrophic agents), cholestatic variants of acute hepatitis A, B, E or alcoholic hepatitis.

Hereditary transport defects

Several monogenetic, hereditary cholestatic syndromes can now be attributed to specific mutations of individual hepatobiliary transport genes. Mutations in specific canalicular ATP-binding cassette (ABC) transporter genes result in syndrom of progressive familial intrahepatic cholestasis and benign recurrent intrahepatic cholestasis. PFIC–1 (Byler's disease) and benign recurrent intrahepatic cholestasis (Summerskill syndrome) are caused by mutations in the ATB8B1 gene encoding an P-type ATPase. PFIC–2 is caused by mutations in the ABCB11 gene encoding the canalicular bile salt export pump. Mutations of the ABCC2 gene encoding the bilirubin conjugate export pump MRP2 cause Dubin-Johnson syndrome. Mutations in the ABCC7 gene encoding cystic fibrosis.

Acquired Transport Defects

Primarily hepatocellular forms of acquired cholestasis (e.g., drug –induced cholestasis resulting directly from inhibition of transporter expression and function by drugs) are quite rare, and most cholestatic syndromes of clinical relevance are caused at the bile duct level by their obstruction (e.g., extrahepatic biliary obstruction by stones and tumors) or destruction (e.g., VBDS such as PBC and PSC). Most of the changes in hepatocellular and cholangiocellular transport expression encountered in these conditions are secondary changes, which nevertheless may explain and maintain the ongoing functional impairment of bile secretion in cholestatis. The transporter changes encountered in cholestasis therefore seem to represent a mixture of pro-cholestatic and anticholestatic adaptive alterations.

Diagnosis and Differential Diagnosis

Clinically, intrahepatic, non-mechanical cholestasis must be differentiated from extrahepatic, mechanical obstructive cholestasis. This is usually possible with abdominal ultrasound, which plays a central role in the diagnosis work-up of cholestasis. A careful clinical examination and history also give important diagnostic hints as to the cause of cholestasis. Magnetic resonance cholangiography (MRC) is increasingly replacing diagnostic ERCP a PTC. Work-up of chronic intrahepatic (non-mechanical) cholestasis usually requires further serologic studies (e.g. testing for AMA) and liver biopsy. Genetic testing is not yet widely available.

Primary Biliary Cirrhosis (PBC)

PBC is considered an autoimmune disease based on the presence of anti-mitochondrial antibodies, focal T-cell infiltrates, and selective destruction of small intralobular bile ducts. Patients with PBC produce a specific B- and T- cell response to a single imunodominant autoepitope of pyruvate dehydrogenase complex-E2 (PDC-E2), the major autoantigen in PBC. PDC-E2 or related antigen is expressed on cholangiocytes of small interlobular bile duct, but not in the remaining bile duct system, and may initiate the B- and T- cell response against cholangiocytes. First-degree relatives have a 100-fold increased risk for PBC. Smoking is associated with a 3-fold increased risk for PBC.

Primary Sclerosing Cholangitis (PSC)

The pathogenesis of PSC is poorly understood and is likely to be multifactorial. It must be kept in mind that PSC could represent a mixed bag of different conditions with various etiologies. The close association with inflammatory bowel disease suggests a role for bacterial translocation in the pathogenesis of PSC. In addition to immunological factors, hepatobiliary transport defects resulting in toxic bile could contribute to the pathogenesis of this disease. There exists a possibility that ABCB4 (MDR3) mutations could also play a role in PSC.

Treatment

Ursodeoxycholic acid (UDCA) has been shown to exert anticholestatic effects in a number of cholestatic conditions. The administration of UDCA may be considered in intrahepatic cholestasis of pregnancy, liver disease in cystic fibrosis, chronic graft-versus-host disease, several forms of drug-induced cholestasis, and a number of pediatric cholestatic syndromes including progressive familiar intrahepatic cholestasis.
In PBC, long-term administration of UDCA (13–15 mg/kg/d) is regarded as the first line of treatment. UDCA improves biochemical and histological findings in patients with PBC, delays histological progression and development of liver cirrhosis. Combination UDCA and immunsuppresive agents are under evaluation at present and may be superior to UDCA alone.
In PSC, limited data on medical treatment are available. UDCA (20–30 mg/kg/d) improves biochemical parameters in patients with PSC and has been reported to beneficially affect some histological and cholangiographic features. Endoscopic treatment of dominant bile duct strictures via balloon dilatation and/or transient stenting is recommended.
Treatment of pruritus: cholestyramin 1 x 4 g to 4 x 4 g/d, opioid antagonists, enzyme inductors (rifampicin, phenobarbital), promethazin, plasmapheresis, haemoperfusion.
General measures: reduction ingestion of neutral dietary fats with additional administration of medium-chain triglycerides, substitution of vitamins A, D, E, K and calcium.

008

HELICOBACTER PYLORI ERADICATION—WHICH OF THE HUNDREDS OF SCHEMES ARE SUITABLE FOR CLINICAL PRACTICE?

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Over the 20 years since its emergence, schemes of Helicobacter pylori eradication have evolved into protocols combining agents reducing gastric secretion, bismuth compounds and antibiotics. These protocols are based on principles of the pathophysiology of infection to be confirmed by clinical practice.
H. pylori infection is one of the most widespread infections worldwide afflicting about more than a half of the population. Most infected patients remain asymptomatic throughout their lives while a smaller proportion develops duodenal or gastric ulcers; a fragment of patients develops MALT lymphoma or gastric cancer. In other patients,

H. pylori infection is accompanied by non-specific dyspepsia, asymptomatic gastritis, and/or extragastric manifestation may also develop. The effect of infection and its elimination on these manifestations is sometimes direct and predictable while, in other cases, it is complex, indirect, and unclear. Cure of the infection involves healing of the ulcers and MALT lymphoma as well as prevention of gastric cancer recurrence. Still, the effect of complete eradication on cancer has not been established. The consequences of H. pylori eradication in non-specific dyspepsia, reflux esophagitis, and the use of non-steroidal anti-inflammatory agents are inconsistent. While H. pylori eradication protocols are multiple with numerous pharmacotherapeutic, diagnostic, financial, geographic, and other aspects, its basic principles are universal. It is indicated in patients with a demonstrable hope for complete cure. Ideal therapy must be effective, simple, well tolerated, and free of side effects, with secondary resistance occurring only sporadically. Results of clinical trials provided the basis for guidelines formulated by consensus conferences held by U.S., European, Canadian, and Asian-Pacific Task Forces. Acceptable definitions for successful H. pylori eradication are over 90% in "per-protocol" analysis, and over 80% in "intent-to-treat" analysis. Most experts recognize the following regimens: 1. PPI (proton pump inhibitor) at standard dose or ranitidine bismuth citrate (RBC) 400 mg + clarithromycin (C) 500 mg + amoxycillin (A) 1 g, all t.i.d. for 7 days. 2. PPI or RBC 400 mg + C 500 mg + metronidazole (M) 400 mg administered t.i.d. for 7 days. 3. PPI + A 1 g + M 400 mg, t.i.d. for 7 days. 4. Colloidal bismuth subcitrate (CBS) 120 mg 4 times a day, M 400 mg t.i.d. + tetracycline (TTC) 500 mg 4 times a day for 2 weeks. 5. PPI t.i.d., CBS 120 mg 4 times a day, M 400 mg t.i.d. + TTC 500 mg 4 times a day for 7 days. If therapy fails, the same regimen can be used, or an alternative tried (e.g., option 5). Bismuth compounds are one of the most traditional eradication agents although their exact composition is not clear, and the mechanism of their antibacterial effect is also poorly understood. The more complicated regimens and side effects have made PPI combinations more popular. The same effect can be obtained with H2 receptor antagonists. Generally, amoxycillin-based combinations are preferred to metronidazole, particularly in high-resistance cases. Clarithromycin is a key antibiotic. While most studies with clarithromycin combinations reported high efficacy, bacterial resistance rose to be as high as 15% in some regions. Resistance is a frequent reason for eradication failure, especially so when combined with metronidazole resistance. The risks and consequences of bacterial resistance are reduced by concomitant bismuth administration. The cause of eradication therapy failure is a multifactorial process, with the main factors being, in addition to bacterial resistance, compliance and indication (with results with ulcer superior to those with dyspepsia).

Regimens involving combinations for less than 5 days, administration of several drugs in a single capsule, and alternating antibiotics after several days have also been developed. These regimens have not yet been reviewed by consensus. The guidelines specifying the most appropriate regimens must take into account the target group of physicians they are intended for. Primary eradication is often undertaken by general practitioners. The guidelines should be relatively simple, as it is the motivation of the patient based on a reasonable level of information that is of key importance. Gastroenterologists and, most importantly, experts in H. pylori eradication, are able to select from a whole range of protocols while—needless to say—fully taking into account evidence-based medicine.

009

RESECTION AND DRAINAGE PROCEDURES IN TREATMENT OF PATIENTS WITH CHRONIC PANCREATITIS

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Introduction

Painful jaundice and most often pain are the predominant symptoms that bring patients with chronic pancreatitis to the surgeon. Pain is a certain scale for judgment of the quality of life. The surgical treatment of patients with chronic pancreatitis is based first on the preservation of as much pancreatic function as possible, while attempting to improve the patient's symptoms. Second, it is widely accepted that the operative approach depends on the anatomy of pancreatic duct and the mass of the head of pancreas. Ducts of big diameter require drainage procedures as Partington-Rochelle, Peustow or Frey. However, when the duct is of a small calibre type, resection of the gland is the only option. Some 10 %–20 % of patients develop an inflammatory enlargement of the head of pancreas, which does not exclude the possibility of carcinoma in these patients groups. The surgical options are resection procedures (Whipple type) or duodenum – sparing resection of the pancreatic head (Beger type).

Patients and Methods

During the years 1995–2002, 235 procedures for chronic pancreatitis were performed in the 1st surgery department in Prague. The Partington-Rochelle procedure was performed in twenty five percent of all cases; twelve patients underwent resection of the left side of pancreas and Roux-en- Y loop of jejunum draining the stump of pancreas. The Beger's procedure was carried out in 61 cases and the Whipple procedure in 31 cases.

Results

When we compare the Beger's operation with non-complicated duodenopancreatectomy, the early postoperative complications (pain, malnutrition, physical constitution and social position) are in the same rate. They differ depending on the patient's co-operation. At about 87 % of patients after longitudinal drainage of the duct a satisfactory results were recorded, while at operated patients 78 %. The Frey's operation is accompanied by difficulties with a partial removal of pancreatic head's tissue. Experiences regard the Beger's and Whipple's operation as more logical, for the removal of the main tissue mass of the pancreatic head, responsible for pain, causes complications of fibrosis in the area round the bile duct and duodenum responsible for the deterioration of the compartment syndrome in the left half of the gland.

Septic complications appeared in nine patients (six respiratory and three catether sepsis) and in three cases pancreatic fistulas occurred. The hospital postoperative stay had a median duration of 18 days (range 10–28 days). Complications after the classical Beger's operation as well as hospitalisation duration were shorter by five days on average compare to the classical method of Whipple.

Conclusion

In author's opinion the success of surgery depends on surgeon's experience and natural course of progressing inflammatory illness of pancreas.
The procedure is considered as less recommendable.

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