Indian J Pediatr (November 2016) 83(11):1334–1340
DOI 10.1007/s12098-016-2168-1

REVIEW ARTICLE

Ascites in Children

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Received: 31 August 2015 / Accepted: 19 May 2016 / Published online: 9 June 2016

Abstract Ascites is an accumulation of serous fluid within the peritoneal cavity. It is the most common complication of liver cirrhosis. In children, hepatic, renal and cardiac disorders are the most common causes. Portal hypertension and sodium and fluid retention are key factors in the pathophysiology of ascites. Peripheral arterial vasodilatation hypothesis is the most accepted mechanism for inappropriate sodium retention and formation of ascites. Diagnostic paracentesis is indicated in children with newly diagnosed ascites and in children with suspected complications of ascites. Ascitic fluid is evaluated for cell count, protein level, and culture. The serum-ascites albumin gradient (SAAG) is the best single test for classifying ascites into portal hypertensive (SAAG >1.1 g/dl) and non–portal hypertensive (SAAG <1.1 g/dl). A neutrophil count ≥250 cells/mm^3 is highly suggestive of bacterial peritonitis. The treatment of ascites due to non-liver disease depends on the underlying condition. In liver disease, diuretics as monotherapy or dual therapy and salt restriction form the mainstay of treatment in children with mild to moderate ascites. Fluid restriction is helpful in children with hyponatremia. In non-responsive ascites or in children with large ascites, large volume paracentesis (LVP) with albumin infusion should be performed. In children with refractory ascites, LVP with albumin administration, transjugular intrahepatic porto-systemic shunt (TIPS), peritoneo-venous shunting and liver transplantation are other therapeutic modalities that need to be considered.

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Keywords Ascites · Child · Cirrhosis · Diagnosis · Management

Introduction

Ascites is an accumulation of serous fluid within the peritoneal cavity. It can occur in various disorders, but in children, hepatic, renal and cardiac causes are the most common [1]. It is the most common complication of cirrhosis and a sign of advanced liver disease [2]. Ascites poses an increased risk for infections, particularly spontaneous bacterial peritonitis, as well as renal failure and mortality.

Etiology

Congenital / Neonatal Ascites

Congenital or neonatal ascites is a rare presentation. Commonly associated causes are intrauterine infections, metabolic disorders, disorders of cardiac structure and rhythm, and occasionally, hematological or genitourinary disease (Table 1). Rhesus hemolytic disease is now an uncommon cause due to use of Anti-D immunoglobulin. Liver and metabolic disorders contribute to 4 % of cases [3].

Childhood Ascites

Childhood ascites is a common entity in pediatric practice. Most common causes are related to liver disease (cirrhosis and portal hypertension), cardiac disease (congestive cardiac failure, pericardial disease) and renal system (nephrotic syndrome, renal failure). In India, protein energy malnutrition and tuberculosis are two other common causes that need to be

Table 1 Causes of congenital / neonatal ascites

Lysosomal disorders	Infantile free sialic acid storage disease (Salla disease), Wolmans disease, GM1 Gangliosidosis type I, Niemann Pick Type A & C, Gaucher disease, Mucopolysaccharidosis VII
Metabolic liver diseases	Neonatal hemochromatosis, Alpha 1 anti-trypsin deficiency, Tyrosinemia type I, Mitochondrial disorders
Intrauterine infections	Cytomegalovirus, Toxoplasmosis, Syphilis
Disorders of cardiac structure or rhythm	Congenital heart blocks, Ebstein's anomaly, Hypoplastic left heart syndrome
Hematological	Homozygous alpha thalassemia, Rhesus hemolytic disease
Genitourinary	Congenital nephrotic syndrome, Posterior urethral valve
Chromosomal disorders	Down's syndrome, Turner's syndrome, Edward's syndrome, Patau's syndrome

considered. Other uncommon causes are related to vascular system (hepatic venous outflow disease), pancreas (severe acute pancreatitis, pancreatic trauma causing duct rupture, biliary system (perforation of choledochal cyst or bile ducts, post biliary surgery), endocrine (hypothyroidism), gastrointestinal infections (tuberculosis), neoplasms, lymphatic obstruction or trauma.

Pathophysiology

Two important factors are required for development of ascites in liver disease. Portal hypertension secondary to liver cirrhosis leads to hepatic venous outflow block leading to congestion within the hepatic sinusoids and subsequent leakage of fluid into the peritoneum. The other crucial factor is inappropriate sodium and water retention allowing for the replenishment of the intravascular volume and maintenance of ascites formation. This sodium retention is either as a primary event (overfill hypothesis) or secondary to vascular changes (underfill and peripheral vasodilatation hypothesis) [4, 5].

Peripheral Vasodilatation Hypothesis

Arterial vasodilatation occurs possibly secondary to nitric oxide production [6]. Some other vasodilators like adrenomedullin, carbon monoxide, endocannabinoids, prostacyclin, tumor necrosis factor alpha and urotensin have also been implicated. Peripheral arterial vasodilatation results in a reduction in effective arterial blood volume and a decrease in systemic arterial pressure, leading to the activation of the renin–angiotensin–aldosterone system (RAAS) and the sympathetic nervous system. This causes sodium and water retention and renal vasoconstriction leading to plasma volume expansion and ascites in the background of portal hypertension.

Overflow Hypothesis

This theory proposes that the primary event is renal in origin. A signal arising from the liver results in a primary increase in plasma volume through increased renal sodium and water retention, an increase in cardiac output and a fall in systemic vascular resistance. These signals have been postulated to be reduced hepatic synthesis of a natriuretic agent, reduced hepatic clearance of a sodium-retaining hormone, or a 'hepatorenal reflex' of unknown etiology.

Clinical Features

Accumulation of ascites is associated less frequently with peripheral edema in children than in adults. The first indication of ascites formation in children is inappropriate weight gain. In early ascites, the only other abnormality might be dullness on percussion in the flanks. As more fluid accumulates, the presence of ascites eventually might be notable by inspection alone. If the patient is in a supine position, the fluid is first visible as bulging flanks. Later, the abdomen becomes grossly distended and umbilicus is everted due to increased abdominal pressure. In gross ascites, the skin is shiny and the increased intra-abdominal pressure leads to umbilical, inguinal, femoral or incisional hernias and divarication of recti. Abdominal striae may be seen. Dilated abdominal collaterals and caput medusa may be seen in ascites due to liver disease while collaterals in flanks and at back are suggestive of inferior vena cava block. Shifting dullness, fluid thrill and Puddle sign are other tests to detect fluid in the abdomen. Positive fluid thrill is a more specific but late sign of gross and tense ascites. Absence of shifting dullness or of fluid thrill or both does not exclude a diagnosis of ascites as the above two signs can be elicited in only about half of the cases of ascites. Elevated jugular venous pressure may suggest constrictive pericarditis as an etiology. Patients with cardiac disease or nephrotic syndrome may have anasarca. Right sided pleural effusion may be seen in some cirrhotic patients due to defects in diaphragm. Ascites can be graded as Grade 1 (Mild) — Detected on USG only, Grade II (Moderate) — Evident by moderate symmetrical distension of abdomen and Grade III (Large/Gross) — Marked abdominal distension [7].

Diagnosis of Ascites

Radiology and Imaging Studies in Ascites

Plain Abdominal Radiograph

Although not necessary for the diagnosis of ascites, it may show signs of ascites, including displacement of the colon from the properitoneal flank stripe, centrally located floating small bowel loops, separation of bowel loops or fluid lateral to the liver or spleen. The presence of fluid in the pelvis causes increased density above the bladder, producing the so-called dog-ears sign.

Abdominal Ultrasonography

It is a sensitive test to detect the presence of ascites. As the amount of fluid increases it is detectable in the pericolic gutters (Morison's pouch) and around the liver and spleen. Echoes within the fluid suggest the presence of exudates, clotted blood or malignancy.

Computed Tomography and Magnetic Resonance Imaging

These are not recommended for confirming the diagnosis of ascites, although they may help to determine the cause in certain situations.

Diagnostic Paracentesis

It is an essential procedure in the diagnostic assessment of patients to determine various etiologies and to rule out complications such as spontaneous bacterial peritonitis that requires analysis of the ascitic fluid for the diagnosis. Paracentesis is typically performed through the abdominal wall in the left lower quadrant. In the midline, cephalad or caudad to the umbilicus, abdominal wall collateral vessels may be present, so these areas should be avoided. The anterior superior iliac spine should be located and a site is chosen that is two fingerbreadths (3 cm) medial and two fingerbreadths (3 cm) cephalad to this landmark [8]. Indications for diagnostic paracentesis include (1) New onset ascites (2) Cirrhotic patients with ascites on admission (3) Cirrhotic patients with ascites and clinical signs of infection (4) Cirrhotic patients with ascites and unexplained deterioration [9].

Gross Appearance

Ascitic fluid is typically translucent and yellow. Fluid of other color or consistency reflects specific underlying disease processes (Table 2).

Table 2 Gross appearance of ascites according to the disorder

Ascitic fluid color	Disorder
Clear or Pale	Portal hypertension
Blood stained	Malignancy, abdominal trauma, invasive investigation such as liver biopsy or transhepatic cholangiography
Turbid or Purulent	Pyogenic peritonitis
Chylous (Milk colored)	Cirrhosis, Thoracic duct injury, Lymphoma
Black/ Tea color	Pancreatic ascites
Brown	Hyperbilirubinemia (most common), Gallbladder or biliary perforation, Choledochal cyst

Ascitic Fluid Neutrophil Count and Culture

Spontaneous bacterial peritonitis (SBP) may be present in approximately 10–30 % of patients with cirrhotic ascites [10, 11]. An ascitic neutrophil count of ≥250 cells/mm^3 is diagnostic of SBP in the absence of bowel perforation [12]. Overall culture positivity is 40–60 % by routine methods, however, bedside inoculation of 10 ml of ascitic fluid directly in blood culture bottles increases positivity by 90 % [13].

Gram Stain

Since the median bacterial concentration of ascitic fluid is very low, Gram stain of ascitic fluid may not be particularly helpful. Gram stain positivity in SBP is less than 10 %. Its role is primarily when secondary bacterial peritonitis secondary to bowel perforation is suspected, where multiple organisms are seen on Gram's stain.

Other Ascitic Fluid Parameters

In certain clinical situations, specific investigations like triglyceride levels, amylase levels *etc.* in the ascitic fluid could point to certain disorders (Table 3).

Serum-Ascites Albumin Gradient (SAAG)

The SAAG is calculated by subtracting the ascitic fluid albumin value from the serum albumin value, and it correlates directly with portal pressure. The SAAG is the best single test for classifying ascites into portal hypertensive (SAAG >1.1 g/dl) and non–portal hypertensive (SAAG <1.1 g/dl) causes with an accuracy of approximately 97 % [14]. A high gradient is associated with diffuse parenchymal liver disease, hepatic venous outflow disease, liver metastasis and hypothyroidism (Table 4). There are some limitations of SAAG: (a) SAAG may be falsely low in presence of low serum albumin (<1.1 g/dl), and in hypergammaglobulinemia (>5 g/dl); b) Errors may occur if the

Table 3 Specific investigations on ascitic fluid

Investigation	Levels	Interpretation
Triglyceride	Increased (>200 mg/dl)	Chylous ascites
Amylase	Increased (>1000 IU/L) or Five times serum level	Pancreatitis, pancreatic trauma
Glucose	Decreased	Tuberculous and bacterial peritonitis
Alkaline phosphatase	Increased (> 240 IU/L)	Small bowel perforation, hollow viscous trauma
Bilirubin	Increased (> 6 mg/dl) and more than serum bilirubin	Biliary ascites (ruptured choledochal cyst), perforation of bile ducts
Adenosine Deaminase (ADA)	Increased (> 20–40) U/L	Tuberculous ascites

samples are not drawn simultaneously or if the patient is in shock; (c) SAAG may be falsely high in chylous ascites as lipids tend to interfere with albumin estimation [15].

Spontaneous Bacterial Peritonitis

This is a serious complication of ascites. It refers to bacterial peritonitis not associated with gut perforation or any other "secondary" source. Characteristically, SBP in children is caused by a single species such as Klebsiella spp., *E. coli*, Enterococcus, *Streptococcus pneumoniae* and recently methicillin resistant *Staphylococcus aureus* [16, 17]. Other variants of bacterial fluid infection in cirrhotic children are given in Table 5. Multiple organisms are usually seen when bowel perforation and secondary peritonitis has occurred. SBP should be suspected in a patient with ascites with concurrent fever, abdominal pain, or elevated white blood cell count, worsening encephalopathy and hypotension. The diagnosis depends on a positive ascitic fluid culture, without an apparent surgically treatable source of infection. If SBP is suspected, empiric treatment should be started in all children with an elevated neutrophil count in ascitic fluid. Cefotaxime is the antibiotic of choice as it is effective against the organisms isolated and has good concentration in ascitic fluid. Other antibiotics like ceftriaxone and co-amoxiclav are also effective. Duration of treatment is 5–7 d. Infusing 1.5 g albumin/kg at the time of diagnosis, followed by 1 g/kg on day 3, is helpful in reducing renal impairment and improving survival [18]. Follow up paracentesis is indicated whenever secondary peritonitis is suspected, or whenever there is poor response to antibiotics. Long term administration of oral norfloxacin (5–7.5 mg/kg/d) once daily is recommended in cirrhotic patients who have recovered from the first episode of SBP and short term prophylaxis during an episode of acute upper gastrointestinal hemorrhage [9, 19].

Table 4 Diagnostic usefulness of SAAG

High gradient (≥1.1 g/dl)	Low gradient (< 1.1 g/dl)
Cirrhosis	Tuberculosis
Hepatic venous outflow disease	Nephrotic syndrome
Cardiac ascites	Pancreatic ascites
Fulminant hepatic failure	Biliary ascites
Massive liver metastasis	Bowel obstruction
Myxoedema	Connective tissue disease
	Post operative lymphatic leak

Management of Uncomplicated Ascites

The treatment of ascites unrelated to portal hypertension depends on the underlying cause. Ascites of nephrotic syndrome responds to salt restriction and diuretics. Tuberculous ascites improves with anti tuberculous medicines. Post traumatic or post surgical lymphatic ascites may require surgery. Pancreatic ascites may be self limiting, may respond to octreotide infusion or may require endoscopic or open surgery. Further discussion is restricted to portal hypertension related ascites. The term 'uncomplicated ascites' is usually used for ascites that is not refractory and not associated with SBP, hyponatremia or Hepatorenal syndrome (HRS). Besides control of ascites, maintenance of adequate growth is an important consideration in treatment of children.

Mild to Moderate Ascites

These children can be treated as out-patients if there are no complications of liver disease. Mild ascites usually requires no specific treatment. In children with moderate ascites, the goal of therapy is achieving a negative sodium balance primarily by sodium restriction and increasing renal sodium excretion by diuretics.

Bed Rest

In children with normal serum sodium, there is little evidence that forced bed rest is helpful in reducing ascites and should not be advised [7].

Sodium Restriction

The evidence for salt restriction in ascites is also limited. Nevertheless most guidelines advise restriction of dietary salt

Table 5 Variants of ascitic fluid bacterial infection in children with liver cirrhosis [2]

S. No	Variants	Absolute PMN count per mm^3	Bacterial culture	Antibiotic treatment required
1.	Spontaneous bacterial peritonitis	≥ 250	Positive for a single organism	Yes
2.	Culture-negative neutrocytic ascites (CNNA) - No antibiotics in last 7 d - No other cause	≥ 250	Negative	Yes
3.	Polymicrobial bacterascitis	< 250	Positive	Yes

PMN Polymorphonuclear

in children with ascites [7]. Daily intake of salt (NaCl) can be half a teaspoon (2-3 g/d) or 1–2 mEq/kg/d in older children and adolescents but in smaller children and infants, salt (NaCl) intake should not be >1 g/d (quarter teaspoon daily). Salty snacks and added salt during meals is to be avoided like pickles, chips, sauces, sea fish *etc.* Addition of sweet to foodstuffs will help children to overcome problems of salt restriction. One hundred fifty cal/kg/d comprising high carbohydrate 60 %, protein (vegetable protein) 15 % and fat 30–35 % should be provided. Prophylactic salt restriction is not recommended in children who have never developed ascites. Fluid restriction is only needed when there is dilutional hyponatremia (Na <120 mEq/L) [7].

Diuretics

Commonly used diuretics in children are aldosterone antagonists (spironolactone) and loop diuretics (furosemide). Spironolactone is more effective than furosemide, but has a slower onset of action [20]. Hence dose of spironolactone is increased every 3–5 d. Dual therapy with spironolactone and furosemide causes early mobilization of fluid, shortens hospitalization and maintains normokalemia and is recommended as initial therapy in patients with recurrent ascites [7, 21]. Dual therapy can be changed over to monotherapy with spironolactone alone after obtaining satisfactory response. However for children with the first episode of ascites, monotherapy with spironolactone alone may be preferred. Nearly 90 % of patients respond to treatment while on salt restriction and diuretics. The goal of treatment is a negative fluid balance of > = to 10 ml/kg/d or weight loss of 0.5 kg/d. Higher negative balances may lead to plasma volume depletion and reduced renal function. On resolution of ascites, diuretic dose should be reduced and stopped if possible. Diuretics should be used cautiously in children with renal impairment or electrolyte disturbances. They should be discontinued in presence of severe hyponatremia (serum sodium concentration < 120 mmol/L), worsening renal failure or hepatic encephalopathy. Furosemide should be stopped if there is severe hypokalemia (<3 mEq/L) and spironolactone, in severe hyperkalemia (serum potassium >6 mEq/L). Regular monitoring is needed to determine the optimum diuretic doses and prevention of complications like azotemia, severe potassium and sodium abnormalities, plasma volume depletion and hepatic encephalopathy. Daily monitoring involves monitoring weight, abdominal girth, peripheral edema, sensorium, input and output records, 24-h urine sodium excretion value or spot urine sodium/potassium ratio (since 24 h urine collection is cumbersome in children), and daily blood biochemistry value of sodium, potassium and creatinine.

Spironolactone It is a potassium sparing aldosterone antagonist having a prolonged half life (5–7 d) and delayed onset of action. It acts at aldosterone-sensitive-sodium channels in the distal renal tubules and collecting ducts and inhibits aldosterone secretion. Spironolactone is best given with food and its effect is observed in 48–72 h. Spironolactone therapy may be complicated by hyperkalemia, hypochloremic acidosis, hypersensitivity reactions and tender gynaecomastia. Starting dose of spironolactone is 1–3 mg/kg/d upto a maximum of 6 mg/kg/d, preferably as a single morning dose to ensure better compliance.

Furosemide It is a loop diuretic acting at the ascending loop of Henle where maximum amount of sodium filtered by the kidney is reabsorbed. It prevents reabsorption of sodium and water and delivers them to the distal convoluted tubules by inhibiting the sodium-potassium-2 chloride binding co-transport system and thereby increasing excretion of water. The dose is 1–2 mg/kg/d to a maximum dose of 6 mg/kg/d. Depending on the response, dose is stepped-up by 0.5 to 1 mg/kg/d and is usually given in 2 doses in the morning and noon. Oral or parenteral IM/IV dose should not exceed 1 mg/kg/6 hourly and should be given under supervision. Side effects include hyponatremia, hypokalemia, hyperuricemia, hyperglycemia, tinnitus, deafness, and hypersensitivity reactions.

Large (Gross) Ascites

Large volume paracentesis (LVP) with albumin infusion is the preferred treatment in large ascites. It is defined as removal of 50 ml or more of ascitic fluid/kg of dry body weight [22]. Around 100–150 ml/kg of ascitic fluid can be safely removed in one sitting [22]. LVP is usually done with 20 % albumin infusion and frusemide on a daily basis with careful

monitoring of electrolytes. In adults, LVP has been shown to be more effective, safer and shortens hospitalization compared to diuretics alone [7]. However LVP may be associated with post paracentesis circulatory dysfunction (PPCD), a condition characterized by a reduction of effective blood volume. This can be prevented by a slow infusion of albumin in doses of 0.5-1 g of albumin/kg or 1 g of albumin/100 ml of ascitic fluid removed over 2–4 h [22]. Albumin infusion can be started at beginning or end of LVP when the volume of ascites removed is known. Albumin replacement is more effective than the other less costly intravenous colloids (plasma expanders) [23]. LVP has no effect on renal sodium and water retention and hence diuretics need to be continued after fluid removal to prevent re-accumulation. LVP should be avoided in children with associated disseminated intravascular coagulation. Routine prophylactic use of fresh frozen plasma or platelets before paracentesis is not recommended. However some centers use them in the presence of severe coagulopathy (prothrombin activity less than 40 %) or thrombocytopenia (less than 40,000) respectively [10].

Management of Refractory Ascites

Refractory ascites is ascites unresponsive to sodium restricted diet and high dose diuretic treatment. Refractory ascites cannot be mobilized or recurs early after therapeutic paracentesis and is not preventable satisfactorily by medical therapy. There are 2 types of refractory ascites (1) Diuretic resistant: Ascites that cannot be mobilized or whose early recurrence cannot be prevented due to a lack of response to sodium restriction and diuretic treatment and (2) Diuretic intractable ascites: Ascites that cannot be mobilized or early recurrence cannot be prevented because of the development of diuretic induced complications that prevent the use of an effective diuretic dosage [24]. Ascites associated with Budd-Chiari syndrome is often diuretic intractable. In these situations, LVP with albumin administration (as discussed above), transjugular intrahepatic porto-systemic shunt (TIPS), peritoneo-venous shunting and liver transplantation need to be considered.

Transjugular Intrahepatic Porto-Systemic Shunt (TIPS)

TIPS is a non-surgical portocaval anastomosis and behaves like a side-to-side portacaval shunt. In this procedure, a tract is created between branches of hepatic and portal veins, resulting in an intrahepatic porto-systemic shunt with a concomitant reduction in portal pressure. TIPS reduces the activity of renn in-angiotensin-aldosterone system (RAAS) and increases the natriuretic and glomerular filtration rate (GFR) and thereby causes reduction in diuretic requirements and substantially reduces the need for subsequent paracentesis. Significant reduction in ascites is noted 1–3 mo after TIPS. It has been shown to be more effective than LVP in preventing recurrence of ascites, however development of hepatic encephalopathy can occur in 30–50 % of the patients after TIPS [25–27]. Other complications include shunt thrombosis and stenosis. TIPS is avoided in patients with severe liver/renal failure, concomitant active infection, or severe cardiopulmonary diseases. Hence TIPS remains a second line choice in the treatment of refractory ascites and is reserved for patients who require frequent paracentesis and have reasonable hepatic reserve with normal or minimal renal dysfunction.

Peritoneo-Venous Shunt (PVS Shunt)

PVS is a mechanical device that allows the ascitic fluid to pass from the peritoneal cavity into the general circulation *via* internal jugular vein and superior vena cava (SVC) using a special plastic tubing and a unidirectional pressure sensitive valve. Flow is maintained by the pressure gradient between peritoneal cavity and SVC. This technique produces a marked increase in plasma volume and inhibits renin, aldosterone, noradrenaline and antidiuretic hormone (ADH) concentrations leading to an increase in diuresis, natriuresis and free water clearance. Renal function and nutrition improve. However PVS is associated with many complications like disseminated intravascular coagulation, leakage of ascitic fluid, variceal bleeding, congestive cardiac failure, pulmonary edema and sepsis. Perioperative mortality varies from 20 to 50 %. Shunt dysfunction or thrombosis may be inevitable. Due to these complications, PVS has a limited role in the management ascites and may be considered when TIPS is contraindicated and as a bridge to liver transplantation. [28, 29].

Liver Transplantation (LT)

LT is the only life saving modality of treatment for all end stage liver disease patients with refractory ascites. Outcome is better when LT is done before development of hepato-renal syndrome and in those who did not undergo surgical porto-systemic shunting.

Contributions AB: Literature review, manuscript review, editing and will act as guarantor for the paper; NT: Literature search, manuscript drafting, review and editing.

Compliance with Ethical Standards

Conflict of Interest None.

Source of Funding None.

References

1. Kennedy M, Liacouras CA. Ascitis. In: Kliegman RM, Stanton BF, Geme JW, Schor NF, Behrman RE, editors. Nelson textbook of pediatrics. New Delhi: Elsevier Saunders; 2012. p. 5041–4.

2. Sankaranarayanan VS. Ascites in children. In: Bavdekar AR, Mathai J, Malathi S, Yachha SK, editors. IAP Speciality series on pediatric gastroenterology. New Delhi: Jaypee; 2013. p. 270–80.
3. McKiernan PJ. The acutely ill baby. In: Kelly D, editor. Diseases of the liver and biliary system in children. Birmingham: Wiley-Blackwell; 2008. p. 106–26.
4. Garcia-Tsao G. Ascitis. In: Dooley JS, Lok ASF, Burroughs AK, Heathcote EJ, editors. Sherlock's disease of the liver and biliary system. Birmingham: Wiley-Blackwell; 2011. p. 210–33.
5. Schrier RW, Arroyo V, Bernardi M, et al. Peripheral arterial vasodilation hypothesis—a proposal for the initiation of renal sodium and water retention in cirrhosis. Hepatology. 1988;8:1151–7.
6. Wiest R, Groszmann RJ. The paradox of nitric oxide in cirrhosis and portal hypertension: too much, not enough. Hepatology. 2002;35:478–91.
7. European Association for the Study of Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol. 2010;53:397–417.
8. Oelsner DH, Caldwell SH, Coles M, Driscoll CJ. Subumbilical midline vascularity of the abdominal wall in portal hypertension observed at laparoscopy. Gastrointest Endosc. 1998;47:388–90.
9. Shepherd R. Complications and management of chronic liver disease. In: Kelly D, editor. Diseases of the liver and biliary system in children. Birmingham: Wiley-Blackwell; 2008. p. 351–78.
10. Rimola A, Garcia-Tsao G, Navasa M, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. J Hepatol. 2000;32:142–53.
11. Larcher VF, Manolaki N, Vegnent A, et al. Spontaneous bacterial peritonitis with chronic liver disease: clinical features and etiologic factors. J Pediatr. 1985;106:907–12.
12. Albillos A, Cuervas-Mons V, Millan I, et al. Ascitic fluid polymorphonuclear cell count and serum to ascites albumin gradient in the diagnosis of bacterial peritonitis. Gastroenterology. 1990;98:134–40.
13. Runyon BA, Antillon MR, Akriviadis EA, McHuchison JG. Bedside inoculation of blood culture bottles with ascitic fluid is superior to delayed inoculation in the detection of spontaneous bacterial peritonitis. J Clin Microbiol. 1990;28:2811–2.
14. Runyon BA, Montano AA, Akriviadis EA, et al. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. Ann Intern Med. 1992;117:215–20.
15. McHutchison JG. Differential diagnosis of ascites. Semin Liver Dis. 1997;17:191–202.
16. Fernández J, Navasa M, Gómez J, et al. Bacterial infections in cirrhosis: epidemiological changes with invasive procedures and norfloxacin prophylaxis. Hepatology. 2002;35:140–8.
17. Cholongitas E, Papatheodoridis GV, Lahanas A, et al. Increasing frequency of gram-positive bacteria in spontaneous bacterial peritonitis. Liver Int. 2005;25:57–61.
18. Narula N, Tsoi K, Marshall JK. Should albumin be used in all patients with spontaneous bacterial peritonitis? Can J Gastroenterol. 2011;25:373–6.
19. Gines P, Rimola A, Planas R, et al. Norfloxacin prevents spontaneous bacterial peritonitis recurrence in cirrhosis: results of a double-blind, placebo-controlled trial. Hepatology. 1990;12:716–24.
20. Pérez-Ayuso RM, Arroyo V, Planas R, et al. Randomized comparative study of efficacy of furosemide versus spironolactone in nonazotemic cirrhosis with ascites. Relationship between the diuretic response and the activity of the renin-aldosterone system. Gastroenterology. 1983;84:961–8.
21. Runyon BA. Management of adult patients with ascites due to cirrhosis. Hepatology. 2004;39:841–56.
22. Kramer RE, Sokol RJ, Yerushalmi B, et al. Large-volume paracentesis in the management of ascites in children. J Pediatr Gastroenterol Nutr. 2001;33:245–9.
23. Ginès A, Fernandez-Esparrach G, Monescillo A, et al. Randomized controlled trial comparing albumin, dextran-70 and polygelin in cirrhotic patients with ascites treated by paracentesis. Gastroenterology. 1996;111:1002–10.
24. Arroyo V, Gines P, Gerbes AL, et al. Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. Hepatology. 1996;23:164–76.
25. D'Amico G, Luca A, Morabito A, et al. Uncovered transjugular intrahepatic portosystemic shunt for refractory ascites: a meta-analysis. Gastroenterology. 2005;129:1282–93.
26. Albillos A, Banares R, Gonzalez M, et al. A meta-analysis of transjugular intrahepatic portosystemic shunt versus paracentesis for refractory ascites. J Hepatol. 2005;43:990–6.
27. Boyer TD, Haskal ZJ. The role of transjugular intrahepatic portosystemic shunt in the management of portal hypertension. Hepatology. 2005;41:386–400.
28. Moore KP, Wong F, Ginès P, et al. The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club. Hepatology. 2003;38:258–66.
29. Dumortier J, Pianta E, Le Derf Y, et al. Peritoneovenous shunt as a bridge to liver transplantation. Am J Transplant. 2005;5:1886–92.