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Review Literature

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Metabolic Encephalopathy After Surgery Hepatobiliary and Pancreatic Diseases

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Abstract
Metabolic Encephalopathy (ME) is a group of diseases with central nervous system dysfunction caused by a variety of etiologies. According to the etiology, it can be divided into Wernicker's encephalopathy (WE) caused by thiamine deficiency, hepatic encephalopathy (HE) caused by liver dysfunction and eventual ammonia poisoning in patients with cirrhosis, hyponatremic encephalopathy caused by plasma hypotonic due to low serum sodium, uremic encephalopathy (UE) caused by toxin accumulation after renal dysfunction, and dysglycemic encephalopathy caused by excessive blood glucose fluctuation. The pathophysiological mechanism of ME is not the same, but for the clinical symptoms, it all show different degrees of neuro-mental symptoms. The mild manifestations are indifference, irritability, time-space sensory disorders, thinking retardation, mental decline etc., and the serious manifestations are delirium, lethargy, coma. In patients with existing metabolic encephalopathy, treating the disease is not an easy task for every clinician, but prevention of metabolic encephalopathy may be much simpler and the return greater than treatment.

Keywords: Hepatobiliary and Pancreatic Diseases, Surgery, Metabolic Encephalopathy, Wernicker's Encephalopathy, Hepatic Encephalopathy.

Introduction

The etiology and pathophysiological mechanism of ME are diverse, but the clinical symptoms of various ME are very similar. Therefore, it is difficult for us medical workers to make a clear diagnosis, which requires us to explore the etiology, and then treat and prevent according to the possible etiology. In hepatobiliary and pancreatic surgery, postoperative metabolic encephalopathy mainly includes Wernicke's encephalopathy, hepatic encephalopathy, hyponatremia encephalopathy, uremic encephalopathy and dysglycemic encephalopathy. In practice, clinicians do not emphasise enough about the occurrence and development of post-operative ME, and can't do better in diagnosis, treatment and prevention. Through the analysis and introduction of the possible etiologies of 14 cases of ME associated with hepatobiliary and pancreatic diseases after surgery in the aothur's hospital after 2019 (Table 1). Among these 14 patients, the proportion of Wernicke's encephalopathy is 78.6%, hepatic encephalopathy is 14.3%, hyponatremia encephalopathy is 14.3%, uremic encephalopathy is 28.6%, and dysglycemic encephalopathy is 21.4%. And then literature study is carried out combining the cases to find treatment and prevention measures.

	Gen	Age (y)	Main Diagnosis	Operations	Incentives	Symptoms	encephalo pathies
1	F	34	choledocholithiasis with cholangitis	LCBDE LC	chronic vomiting	irritability, numbness of limbs	WE
2	F	69	acute biliary pancreatitis; cholecystolithiasis	LC	chronic vomiting; poor diet	gibberish; fatigue	WE

3	M	60	chronic pancreatitis; pseudocyst pancreas	pancreatic cyst jeanastomosis	fasting; gastrointestinal decompression; long-term TPN	gibberish; the confused sensetive of time-space	WE
4	M	83	ampullary malignancy	WHIPPLE	hepatorenal syndrome; chronic vomiting and fasting	delirium; disturbanc consciousness	UE WE
5	M	50	pancreatic malignancy	gastrojejunostomy, choledochojejunostom	Fasting and chronic vomiting	Numbnes limbs, convulsions	WE
6	F	41	gallstones with cholecystitis	LC; postoperative intestinal fistula and intestinal resection	fasting; long-term TPN	drowsiness; bradyphnisia	WE Dysglycemic encephalopathy
7	M	56	SAP; hepatitis cirrhosis	partial pancreatect and drainage of pancrcysts	fasting,;hepatorenal syndrome	hallucinations; gibberish	UE WE
8	M	69	hepatocellular carcinoma	partial hepatectomy	diuretic	drowsiness; indifferent	HE
9	F	56	malignant of pancreatic head	WHIPPLE; left hepatectomy	fasting; chronic vomiting; long-term TPN	drowsiness; lethargy; delirium	WE Dysglycemic encephalopathy
10	F	72	malignant of pancreatic head	LPD	fasting; chronic vomiting; long-term TPN	irritability; lethargy	WE
11	F	52	gallbladder malignant	partial hepatectomy cholangiojejunostomy	poor diet; chronic vomiting; Large amount abdominal drainage fluid	irritability; unconsciousness; drowsiness	WE Hyponatremic encephalopathy
12	M	61	hepatocellular carcinoma	left half hepatectomy; chemotherapy	liver failure, hepatorenal syndrome	Lethargy; restless and gibberish	HE UE
13	M	56	hepatobiliary cell carcinoma	laparoscopic hemihepatectomy	hepatorenal syndrome; blood glucose waving 4.1-31mmol/L	irritability; delirium	UE Dysglycemic encephalopathy
14	M	62	malignant of pancreatic head	WHIPPLE	fasting; chronic vomiting; gastrointestinal decompression; pancreatic fistula; long-term TPN	confusion; gibberish; delirium	WE Hyponatremic encephalopathy

Explanation: GEN-gender; F-Female; M-Male; SAP-Severe Acute Pancreatitis; LCBDE-Laparoscopic Common Bile Duct Exploration; LC-Laparoscopic Cholecystectomy; WHIPPLE-whipple procedure, and called Pancreaticoduodenectomy; LPD-Laparoscopic Pancreaticoduodenectomy; TPN-Total Parenteral Nutrition; UE-Uremic Encephalopathy; WE-Wernicke's Encephalopathy; HE-Hepatic Encephalopathy.

Table 1: Main information for 14 patients.

Wernicke's Encephalopathy

Wernicke's encephalopathy (WE) is an acute or subacute nervous system disease caused by the lack of thiamine in the body. As early as 1881, it was first proposed and named by German neurologists Karl Wernicke [1]. The original WE is concentrated in patients with a history of alcoholism, presenting with neuro-

psychiatric symptoms. As thiamine has been studied, a number of WE unrelated to alcoholism have been discovered. The causes of Thiamine deficiency in WE are varied, such as alcoholism, AIDS, hemodialysis, malignancies, hyperemesis gravidarum, prolonged vomiting, fasting after abdominal surgery with long-term total parenteral nutrition(TPN) and medical glucose load of any disease [2,3].

Pathophysiology

Thiamine is a cofactor of several key enzymes in the tricarboxylic acid cycle (TCA cycle or Krebs cycle) and pentose phosphate pathway, such as α-oxoglutarate dehydrogenase, pyruvate dehydrogenase, and transketolase-2. In the absence of thiamine, the enzymes in the brain that play a key role in energy metabolism will not be able to do their job, which may lead to tissue damage by inhibiting metabolism in brain regions with high metabolic demands and high thiamine conversion rates and eventually presenting neuropsychiatric symptoms. Due to thiamin deficiency, the activity of thiamin-dependent enzymes will also be decreased. Decreased activity of these enzymes may lead to increased accumulation of toxic intermediates. Since pyruvate metabolism lacks key enzymes and cannot enter the Krebs cycle, and the body's demand for energy has always existed, the metabolism of pyruvate is transferred to the production of lactic acid, which leads to the accumlation of lactic acid in the brain and serum, and ultimately leads to lactic acidosis [4,5] (Figure 1).

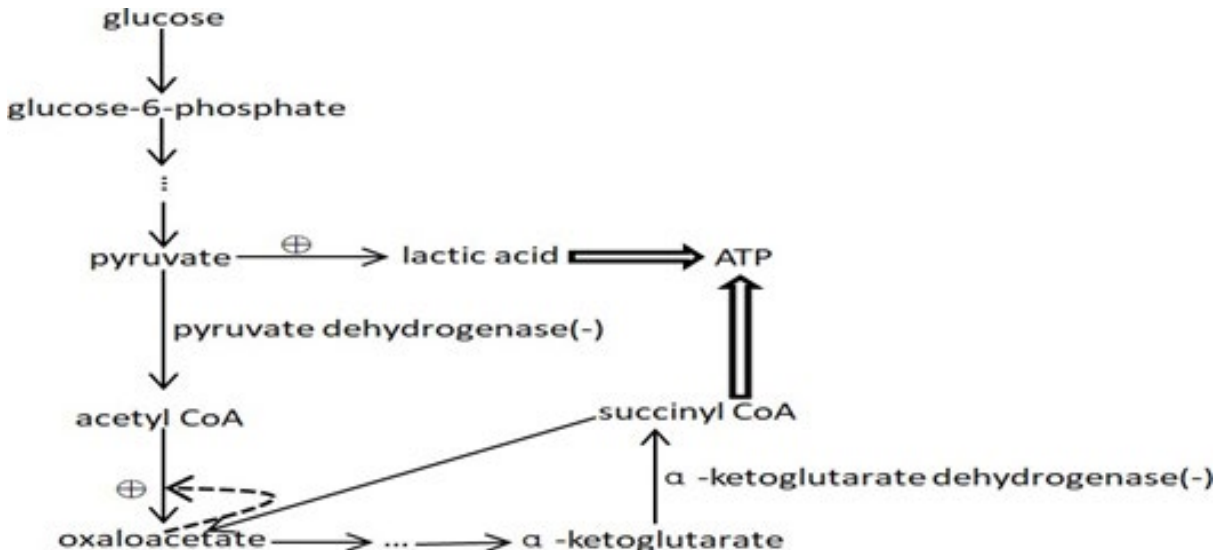

Figure 1: Thiamine involving energy conversion.

There are two main reasons for thiamine deficiency. One is insufficient intake, including insufficient oral intake of patients with normal diet and insufficient iatrogenic supplement in patients with fasting. Another is increased consumption. For a healthy adult, the daily dietary intake of thiamine is generally sufficient to meet the body's needs. Inadequate intake is due to alcohol abuse, inadequate absorption after abdominal gastrointestinal surgery, long-term vomiting, hyperemesis gravidarum, and inadequate thiamine supplementation in enteral or tatol parenteral nutrition. Increased consumption can be attributed to pregnancy, high consumption of systemic infections, and iatrogenic glucose load for any disease. For patients with malignant tumors, the growth of tumors requires a large amount of thiamine, and the patient's intake is also greatly affected, especially for gastrointestinal malignancies, which leads to a serious thiamine deficiency in cancer patients [3,6]. In terms of absorption, the conversion capacity of thiamine in the gastrointestinal tract seems to be different, duodenum and jejunum>colon>stomach [7]. Two thiamine intestinal transporters have been identified: human thiamine transporter-1(hTHTR-1; the product of SLC19A2 transporters) and human thiamine transporter-2 (hTHTR-2; the product of SLC19A3 transporters) [8,9]. Both hTHTR-1 and hTHTR-2 are expressed in the small and large intestines. However, hTHTR-1 shows its maximal expression in the liver [10], followed in order by stomach, duodenum, Jejunum, Colon, and ileum. This transport mechanism is particularly important in hepatobiliary and pancreatic surgery, where partial liver, partial or all duodenum and/or partial stomach are removed, such as radical pancreaticoduodenectomy for pancreatic head or ampullary tumors, and partial liver resection for hepatic malignant tumors.

Manifestations and Diagnosis

The clinical manifestations of Wernicke's encephalopathy are various and nonspecific. The typical triads are ocular abnormalities (nystagmus, partial or total ocular paralysis, and optic neuropathy), ataxic gait disorders, and mental behavioral state changes or memory disorders. However, in clinical cases, the typical triad is rarely seen at the same time. Different from alcoholic Wernicke's encephalopathy, patients with postoperative WE are associated with nutritional metabolism after fasting, and their clinical manifestations are relatively hidden, different from typical triad, most of which are abnormal onset of mental behavior, and changes in mental state and feeling are very common, including irritability, gibberish, apathetic, silent, unable to concentrate, and severe delirium, lethargy, and coma [11]. Studies have shown that the fol-

lowing conditions can be considered as WE. Includes the presence of at least two of the following four conditions: inadequate diet, ocular abnormalities, ataxic gait disorders, and altered mental behavioral states or memory disorders [12]. Insufficient diet is manifested as thiamine deficiency in two aspects: on the one hand, due to the fasting state of the patient, thiamine is not supplemented with sufficient physiological requirements; On the other hand, thiamine absorption is affected because the patients have undergone gastrointestinal surgery.

The serum thiamine level is only a small part of thiamine in the whole body. The detection of thiamine level is mainly through the determination of thiamine diphosphate in erythrocyte lysates by high performance liquid chromatography. However, given the complexity of this test and the delay of experimental results, and the fact that normal levels of thiamine diphosphate do not rule out the diagnosis of WE, it is unwise to use this test when a patient is suspected of presenting with WE [13]. Therefore, the diagnosis of WE is mostly confirmed by clinical manifestations and symptom improvement after thiamine supplementation. When WE is suspected, craniocerebral magnetic resonance imaging (MRI) can detect increased T2 signaling in the paraventricular region of the thalamus and hypothalamus and around the midbrain aquitaquin, while the cerebellum and papillary bodies may become smaller [14]. The sensitivity and specificity of MRI in diagnosing WE were 53% and 93% respectively. But perhaps in patients with a high degree of suspicion of WE, the benefit of MRI is not great and intravenous injection of thiamine ba a better choice.

Treatment and Prevention

Among these 14 patients, the proportion of WE is as high as 78.6%, so doctors should attach great importance to the treatment and prevention of WE. Thiamine is a water-soluble vitamin and the recommended dose for a healthy adult is 1.4mg per day or 0.5 mg per 1000 kcal [15]. The amount of thiamine stored in the body is about 30-50 mg [16]. In the process of traditional rehydration treatment after surgery, most surgeons tend to focus only on the patient's actual calorie requirements or the ratio of sugar, fat and amino acid, while the importance of micronutrients is often ignored. It is necessary for suegeons to provide thiamine supplementation early in high-risk surgical patients, because surgical patients may have many risk factors for thiamine deficiency, such as gastrointestinal surgery, chronic vomiting, malnutrition and high calorie needs. Physicians should also avoid long-term use of high glucose concentrations of TPN, which can lead to increased thiamine requirements [11]. For patients with advanced malignancies, clinicians must be aware of the possibility of thiamine deficiency when unexplained changes in neuropsychiatric symptoms occur with poor nutritional status [17].

In conclusion, it is recommended that when WE is suspected prior to diagnosis, intravenous thiamine 200 mg three times a day until symptoms improve;Patients with multiple risk factors for thiamine deficiency may be given intravenous thiamine 100 mg, once daily or orally in patients with normal gastrointestinal function to prevent progression to WE even if symptoms are not present [18].

Hepatic Encephalopathy

Hepatic encephalopathy (HE) is a serious neuropsychiatric complication caused by incomplete detoxification of portal blood into the brain after hepatocirrhosis or portosystemic shunt. The mechanism of HE currently recognized by the academic community as the toxic effect of ammonia on the nervous system, resulting in clinical manifestations ranging from mild psychiatric symptoms to severe coma [19]. The diagnostic methods of HE is relatively simple and mainly relies on scores of various neuropsychiatric symptoms, such as psychometric hepatic encephalopathy score (PHES). Prevention of hepatic encephalopathy may be more important than treatment. There is no special treatment for hepatic encephalopathy, it is very important to control its high risk factors and prevent HE, so whether it has occurred or not.

Pathophysiology

The pathophysiological mechanisms of HE includes a variety of hypotheses, including the role of neurotoxins, impaired neurotransmitter transmission due to metabolic changes in liver dysfunction, changes in brain energy, systemic inflammatory responses, and changes in the blood-brain barrier [20,21]. Ammonia is the most characteristic neurotoxin associated with HE. The normal functioning liver can remove almost all the ammonia in the portal vein blood flow and convert it into glutamine, preventing it from entering the systemic circulation. Elevated serum ammonia in cirrhotic patients is the result of impaired liver function and blood shunt around liver [20].

Manifestations and Diagnosis

Hepatic encephalopathy has a wide range of nonspecific neurological and psychiatric manifestations, ranging from mild to psychometric changes in attention, working memory, mental agility, and visual-spatial ability to severe to relative personality changes such as apaidity, irritability, and significant changes in consciousness and motor function [22,23]. In severe cases, it can be manifested as progressive exacerbations of temporal and spatial disorientation, such as lethargy, delirium, or even coma [24-26]. The clinical manifestations of hepatic encephalopathy are mostly nonspecific, although elevated blood ammonia levels suggests that the brain dysfunction of patients may be derived from the liver, it is still not specific [27]. Therefore, many factors limit the diagnosis of hepatic encephalopathy. At present, the diagnosis of hepatic encephalopathy still depends on hepatic encephalopathy scoring algorithm. It has been observed that patients with cirrhosis who appear clinically "normal" may also have abnormalities in electroencephalogram (EEG) and neuropsychological tests, the change known as mild hepatic encephalopathy (MHE) [28]. For patients at risk of hepatic encephalopathy, the West-Haven criteria (Table 2) is the gold standard for diagnosis. Which can be diagnosed as MHE if two or more psychological test abnormalities are persent [26]. Several methods can also be used to diagnose MHE [29], including common tests such as Critical Flicker Frequency (CFF), PHES, and EEG. However, this kind of diagnosis methods are still affected by many factors, so that the diagnosis lacks high credibility.

WHC Including MHE	ISHEN	Description	Suggested Operative Criteria	Comment
Unimpaired		No encephalopathy at all, no history of HE	Tested and proved to be normal	
Minimal	Covert	Psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change	Abnormal results of established psychometric or neuropsychological tests without clinical manifestations	No universal criteria for diagnosis local standards and expertise required
Grade I		◆Trivial lack of awareness ◆Euphoria or anxiety ◆Shortened attention span ◆Impairment of addition or subtraction ◆Altered sleep rhythm	Despite oriented in time and space (see below), the patient appears to have some cognitive /behavioral decay with respect to his/her standard on clinical examination or to the caregivers	Clinical findings usually not reproducible
Grade II	Overt	◆Lethargy or apathy ◆Disorientation for time ◆Obvious personality change ◆Inappropriate behavior ◆Dyspraxia Asterixis	Disoriented for time (at least three of the followings are wrong: day of the month, day of the week, month, season, or year) the other mentioned symptoms	Clinical findings variable, but reproducible to some extent
Grade III		◆Somnolence to semistupor ◆Responsive to stimuli ◆Confused ◆Gross disorientation ◆Bizarre behavior	Disoriented also for space (at least three of the following wrongly reported: country, state [or region], city, or place) ± the other mentioned symptoms	Clinical findings reproducible to some extent
Grade IV		Coma	Does not respond even to painful stimuli	Comatose state usually reproducible

Table 2: WHC and Clinical Description.

Treatment and Prevention

In cirrhotic patients, the onset of HE is usually caused by excess nutritional proteins, gastrointestinal bleeding, infection, drugs (especially sedatives or diuretics), or constipation [27]. Therefore, the identification and treatment of predisposing factors should be the first step and primary task of patient management. In addition, it is essential to correct electrolyte disturbance, especially hyponatremia, which increases the incidence of HE as blood sodium levels decrease [30]. Some studies have shown that hyponatremia is a strong predictor of the occurrence of overt HE. Hyponatremia is thought to promote astrocyte swelling in patients with severe liver disease, thereby contributing to the development of HE [31]. Although the clinical presentations of cerebral dysfunction and hepatic encephalopathy associated with hyponatremia are only altered consciousness, every patient should be treated for hyponatremia before neuropsychiatric symptoms are associated with HE [32]. Controlling of predisposing factors are critical in the treatment of overt HE, as correction of predisposing factors can treat nearly 90% of patients [33].

Considering the role of ammonia in the pathogenesis of hepatic encephalopathy, the main primary approach to treatment of HE is to reduce ammonia production and absorption, and to maximize the ability of removing ammonia from the blood [34]. Lactudrop has been shown to reduce blood ammonia levels, improve cognitive function, and reduce interstitium edema in patients with MHE, and it has been shown to be effective in neuropsychological measure scores [35]. Several mechanisms of lactulose: (1) laxative effect; (2) Acidification of intestinal contents reduces ammonia absorption and moves ammonia from blood to intestinal; (3) Reduce ammonia production by bacteria; (4) Interfere with the uptake of glutamine and reduce its metabolism into the intestinal wall of ammonia.The pharmacological mechanism of lactulose can not only reduce the production of ammonia, but also prevent the absorption of ammonia, improving the symptoms of HE in many aspects. Some scholar have shown that lactulose is also effective for secondary prevention in patients with liver cirrhosis complicated with HE [36].

Rifaximin was also effective in the treatment of hepatic encephalopathy, and it significantly reduce the risk of hepatic encephalopathy within 6 months in patients with cirrhosis and decreases the number of hospitalizations for HE by half [37]. Application of L-ornithine-L-aspartic acid can also reduce blood ammonia levels by promoting the urea cycle, thereby reducing ammonia accumulation and accelerating glutamine synthesis in skeletal muscle [38]. For patients with cirrhosis, understanding the risk of HE is helpful for clinical prevention and treatment. Before the operation, the surgoen in charge should understand the patient's liver function, actively remove the inducements of HE and actively prevent the occurrence of it. After the surgery, the surgical complications should be actively treated to the symptoms, such as excessive bleeding, infection prevention, monitoring of blood ammonia level or actively intervening the metabolism of blood ammonia, and when patients are suspected to have latent symptoms of HE, various scoring scales or contacting neurologists for joint diagnosis and treatment, so as to prevent the occurrence of HE or further aggravation of it to the greatest extent [39].

Hyponatremic encephalopathy

Hyponatremic encephalopathy refers to a group of neurological diseases characterized by decreased blood sodium and plasma osmotic pressure, except for the disturbance of consciousness and temporary brain dysfunction caused by central nervous system lesions [40]. Its clinical symptoms vary from nausea, vomiting, headache and ataxia to disturbance of consciousness, seizures and even respiratory arrest. Hyponatremia is a disorder of water and electrolyte with a high postoperative morbidity in patients with hepatobiliary and pancreatic diseases. The etiologies include insufficient sodium supplementation after fasting, large amount of non-sodium glucose supplementation due to high energy needs, long-term vomiting, gastrointestinal decompression, and sodium loss caused by indentation of drainage tube, which is not included in the amount of supplementation or insufficient enough attention, and increased activity of antidiuretic hormone, water and sodium retention in patients with cirrhosis leading to dilutive hyponatremia. When hyponatremia is not properly treated, the disease worsens and eventually develops intohyponatremic encephalopathy.

Pathophysiology

Hyponatremia, in which serum sodium is less than 135 mmol/L, is a reflection of a state of hypoosmosis. Hyponatremia occurs when water intake and excretion are incompatible with sodium intake and excretion. An osmotic gradient forms between blood circulation and brain in the low-sodium state, causing water to enter brain through sodium hydrate channel-4 located in astrocytes [41]. Astrocytes, located onthe brain side of the microcirculation, help regulate the movement of fluids and molecules across the blood-brain barrier through the foot processes where the cells contact with brain capillaries. The movement of this fluid causes swelling of cells and increased brain volume. Since the cerebrospinal fluid can counteract some of the fluctuations in brain volume, slight changes in volume do not cause discomfort. However, the capacity of this volume is limited, and the main regulatory mechanism is the energy-dependent expulsion of solutes from glial cells by the sodium-potassium ATPase, which reduces the osmotic pressure within glial cells, and thus results in an overall reduction in brain volume. This process known as "regulatory brain volume reduction" [42,43]. When these mechanisms do not fully compensate for the cerebral edema caused by hyponatremia, neurological symptoms occur and are referred to as hyponatremic encephalopathy.

Manifestations and Diagnosis

Hyponatremia, a pathophysiological process in which serum sodium is blow 135 mmol/L and causes a range of clinical symptoms of varying degrees [44]. Hyponatremia can be classified as mild (blood sodium 131-134 mmol/L); Moderate (blood sodium 125-130 mmol/L) and severe (blood sodium less than 125 mmol/L) [45]. Hyponatremia is often the result of a combination of etiological factors. Acute hyponatremia, defined as hyponatremia occurring within 48 hours, has obvious clinical symptoms and is prone to cerebral edema [46]. The clinical manifestations of hyponatremic encephalopathy depend on the degree of adaptation of the central nervous system to the hypoosmotic state, and absolute changes in blood sodium alone are not good predictors [47]. The early clinical symptoms of mild hyponatremic encephalopathy include nausea, vomiting, dizziness, attention deficit and ataxia, while the severe clinical manifestations include changes in mental state, altered consciousness, lethargy, delirium, coma, seizures and even respiratory cardiac arrest (Table 3).

Acute severe	Chronic
Nausea and vomiting	Nausea
Headaches	Fatigue
Seizures	Gait and attention deficit
Coma	Falls and bone fractures
Death	
Respiratory arrest	
Noncardiogenic pulmonary edema	

Table 3: Manifestations of hyponatremic encephalopathy.

Some studies have shown that diagnosis of hyponatremic encephalopathy can be started from the following aspects [48]:(1) causes of hyponatremic encephalopathy exist;(2) clinical manifestations of hyponatremic encephalopathy, with obvious disturbance of consciousness and/or neuropsychiatric symptoms;(3) The plasma osmotic pressure decreased significantly, the plasma osmotic pressure less than 250 mmol/L (plasma osmotic pressure=2*(C_{Na+}+C_{Ca2+}+$C_{Glu+}$$C_{BUN}$) has diagnostic significance for hyponatremia encephalopathy;(4) hyponatremia;(5) Exclude the cerebral dysfunctions caused by central nervous system infection, epilepsy or high fever. In patients with postoperative hepatobiliary and pancreatic diseases, most of the above factors will exist. For these patients, we need to do is to remove these risk factors. Patients without the above factors for the development of hyponatremic encephalopathy should be actively prevented from developing it.

Treatment and Prevention

There is no correlation between serum sodium concentration and clinical symptoms, but it has some suggestive effect. Studies have shown that if blood sodium concentration decreases at a rate of less than 0.5 mEq/L per hour over 24 hours, the clinical presentation may not be very serious. However, if blood sodium concentration decreases at a rate greater than 1.0 mEq/L per hour, serious clinical manifestations, even neurological sequelae and death are often observed [49]. Treatment of mild and moderate hyponatremia encephalopathy depends on the etiology of hyponatremia and is based on adjusting the numerator or denominator of the Edelman equation ($[Na+]_{pw}$=1.11*(Na_e+K_e)/TBW-25.6, $[Na^+]_{pw}$ Plasma water sodium concentration; K^+_e Exchangeable potassium; Na+e Exchangeable sodium; TBW Total Body Water.) to restore normal serum sodium concentration [50]. When severe hyponatremia encephalopathy is identified, the recommended dosage and dosing schedule varies according to differet guidelines, but it is generally accepted that 500 ml 3% sodium chloride injection should be administered at 100 ml per hour and that this method is safe [51,52]. Intravenous treatment with 3% sodium chloride injection is recommended when early symptoms occur, rather than waiting for advanced symptoms to develop, as delayed treatment is associated with a poorer neurological prognosis [53]. The goal of this initial treatment is rapid treatment of severe cerebral edema. The correction of blood sodium should not exceed 5 mmol/L during the first 1-2 hours of treatment. It is recommended to increase blood sodium concentration by less than 10 mmol/L during the first 24 hours and by another 8 mmol/L every 24 hours until blood sodium reaches 130 mmol/L. Blood sodium should not change more than 15-20 mmol/L during the first 48 hours of treatment.

For the prevention of hyponatremic encephalopathy, it is very important to remove the causes of hyponatremia, such as long-term postoperative abrosia, the need to replenish a lot of energy and the infusion of non-sodium glucose resulting in dilutive hyponatremia, long-term vomiting, gastrointestinal decompression and indplacement of drainage tube leading to the loss of sodium in the body and not included in the amount of supplement or insufficient attention, and long-term ascites loss and increased activity of antidiuretic hormone or the use of diuretics resulting in water and sodium retention or loss of serum sodium resulting in hyponatremia in patients with cirrhosis [54]. In addition, gender, age, and hypoxia are three major clinical risk factors that predicted poor outcomes more than the incidence of hyponatremia or absolute decline in serum sodium [55,56]. Estrogen is thought to inhibit neuronal astrocyte sodium-potassium ATPase activity, leading to regulatory volume reduction of functional impairment [57]. Hypoxia has been shown to predict poor outcomes in patients with hyponatremia encephalopathy because it also impairing the energy-dependent sodium-otassium ATPase that brings solutes out [58].

In conclusion, although hyponatremic encephalopathy is not prone to neurological sequelae, when severe hyponatremia occurs, we should actively seek the cause and prevent its further progression to hyponatremic encephalopathy.

Uremic Encephalopathy-Hepatorenal Syndrome

Uremic encephalopathy (UE) refers to a series of central nervous system abnormalities associated with renal dysfunction due to chronic kidney disease (CKD) or acute kidney injury (AKI), and it is an ill-defined complex syndrome of cognitive and nervous system dysfunction [59]. First proposed by Richard Bright in 1831, uremic encephalopathy is classified as metabolic encephalopathy. This syndrome may be caused by uremic solute retention, nutrient deficiency, electrolyte and acid-base balance changes, as well as changes in vascular reactivity and blood-brain barrier transport permeability [60]. The typical clinical manifestations of UE are psycho-nervous system changes, including inattention, memory loss, depression, and lethargy.Even seizures or coma [61,62]. In patients with postoperative hepatobiliary and pancreatic diseases, two cases were considered as uremic encephalopathy due to hepatorenal syndrome (HRS).This review will focus on uremic encephalopathy caused by HRS. Hepatorenal syndrome is an extreme manifestation of renal function damage in cirrhotic patients, characterized by reduced renal blood flow and glomerular filtration rate, with high morbidity and mortality [63]. HRS is subdivided into two clinical types: one is defined as a rapid decline in renal function, with an initial doubling of creatinine clearance to at least 2.5 mg/dl at 24 hours or a 50% reduction to less than 20 mg/dl in less than two weeks;The other type has renal function progression that does not meet the criteria for the former type [64]. With the progress of scientific research, the classification and nomenclature of HRS have been updated (Table 4) [65]. An important diagnostic criterion for hepatorenal syndrome, which leads to AKI, is the exclusion of structural kidney injury, which depends on microscopic examination of urine and calculation of urinary sodium excretion. Prerenal azotaemia is a major cause of AKI in cirrhotic patients due to frequent use of diuretics without albumin support, gastrointestinal bleeding and/or loss of gastrointestinal fluid because of secondary diarrhea [66,67]. HRS is diagnosed when cirrhotic patients present with ascites and renal dysfunction but lack evidence of intrinsic renal disease such as hematuria, proteinuria, or renal ultrasound abnormalities.When hepatorenal syndrome is not corrected in time, further accumulation of toxins leads to brain dysfunction, which develops into UE.

Old name	New name
HRS type 1 ☞Doubling of serum creatinine to concentration 22.5mg/dl within 2 weeks. ☞No response to diuretic withdrawal and 2 days fluid challenge with 1 g/kg/day of albumin 20-25%. ☞Cirrhosis with ascites. ☞Absence of shock. ☞No current or recent use of nephrotoxic drugs (NSAIDs,contrast dye, etc) ☞No signs of structural kidney injury -Absence of proteinuria (500mg/day) -Absence of hematuria (50RBCs per high power field) -Normal findings on renal ultrasonography.	HRS-AKI ☞Increase in serum creatinine of≥0.3mg/dl within 48 hours or Increase in serum creatinine≥1.5 times from baseline (creatinine value within previous 3 months,when available. may be used as baseline, and value closest to presentation should be used) ☞No response to diuretic withdrawal and 2 days fluid challenge with 1g/kg/day of albumin 20-25% ☞Cirrhosis with ascites ☞Absence of shock ☞No current or recent use of nephrotoxic drugs (NSAIDs, contrast dye, etc) ☞No signs of structural kidney injury -Absence of proteinuria (＞500mg/day) -Absence of hematuria (＞50RBCs per high power field) -Normal findings on renal ultrasound
HRS type 2 ☞Gradual increase in serum creatinine, not meeting criteria above.	HRS-NAKI HRS-AKD ☞Estimated glomerular filtration rate <60ml/min /1.73m^2 for <3 months in absence of other potential causes of kidney disease ☞Percentage increase in serum creatinine<50% using last available value of out patient serum creatinine within 3 months as baseline value. HRS-CKD ☞Estimated glomerular filtration rate<60ml/min /173m^2 for≥3 months in absence of other potential causes of kidney disease.
Previous and current defnitions of hepatorenal syndrome (HRS): AKD=Acute Kidney Disease; AKI=Acute Kidnev Injury;,CKD=Chronic Kidney Disease; NAKl=Non-acute Kidney Injury; NSAlD=Non-steroidal Anti-inflammatory Drug; RBC=Red Blood Cell.	

Table 4: New name and classification of hepatorenal syndrome.

Pathophysiology

Human have limited understanding of the pathophysiological mechanism of hepatorenal syndrome, which mainly comes from observational studies on human diseases. The possible mechanisms are as follows:

Hemodynamic Disorder

Hemodynamic changes in cirrhotic patients are associated with water and sodium retention, ascites, and developing renal dysfunction.Cirrhosis leads to increased intrahepatic vascular resistance, but vasodilators produced by vascular dilation in the visceral circulation, including nitric oxide, carbon monoxide, and prostacyclin, lead to systemic vasodilation, resulting in a decrease in effective circulating blood volume and systemic blood pressure [68]. In addition, systemic vasoconstriction mechanisms, such as the renin- angiotensin system and the sympathetic nervous system, are also involved in the development of HRS [69]. These mechanisms lead to water and sodium retention, impaired free water excretion, and renal vasoconstriction, thereby reducing renal blood flow (Figure 2).

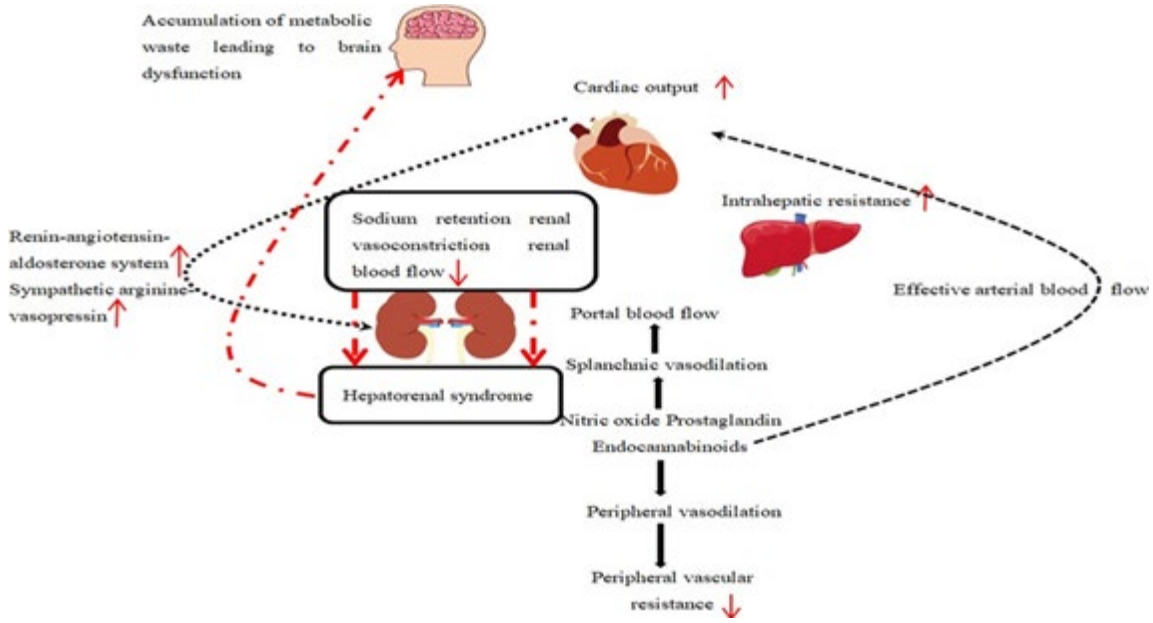

Figure 2: The formation mchanism and toxic accumulation of hepatorenal syndrome.

Elevated abdominal pressure

The abdominal cavity is a closed cavity that is relatively isolated from the outside world. The intra-abdominal pressure is basically 0mmHg under normal circumstances. Elevated abdominal pressure (especially greater than 12 mmHg) is an underreported cause of AHI and may play a role in HRS in patients with refractory ascites. One study showed that creatinine clearance was significantly improved after a reduction in abdominal pressure [70].

Hepato-Adrenal Syndrome

Relative adrenal insufficiency is present in patients with decompensated cirrhosis and ascites and may play an important role in the development of HRS [71,72]. Studies have shown that patients with relatively adrenal insufficiency have lower serum renin and norepinephrine concentrations and lower arterial pressure compared with patients with normal adrenal function.

Hepatorenal reflex hypothesis

It is well known that there is a link between the kidney and liver. This suggests that osmoloreceptors, chemoreceptors and baroreceptors may be present in the liver to influence renal function [73]. One study has shown that activation of intrahepatic adenosine receptors when portal venous blood flow is reduced leads to renal water and sodium retention [74]. This is similar to what has been observed in hepatorenal syndrome, but further studies in human diseases are lacking.

Manifestations and Diagnosis

Consistent with most metabolic encephalopathies, UE has lacks of clinical specificity, with major manifestations including inattention, memory loss, depression, delirium, sleep disturbances, and even seizures or coma [61,62]. Due to the variety of clinical manifestations and lack of corresponding specificity, little attention has been paid to it in clinical application. An important diagnostic criterion for acute kidney injury caused by hepatorenal syndrome (AKI-HRS) is to exclude structural kidney injury, which depends on microscopic examination of urine and urinary sodium excretion.For patients in clinical doubts, lumbar puncture, electroencephalogram (EEG), and imaging can largely rule out other causes. In uremic encephalopathy, the cerebrospinal fluid is usually abnormal, sometimes presenting as a mild increase in cell count and protein concentration. EEG examination lacks specificity and may show systemic decrease with excessive waves βand θ [75]. Some specialists use urinary sodium (greater than 40 mEq/L), partial sodium excretion (FENA greater than 2%), and low urinary osmotic pressure (less than 400 mosm/ L) to indicate acute tubular necrsis (ATN). However, urinary sodium may be associated with patients on diuretics. Therefore, urinary sodium and partial sodium excretion cannot be used as diagnostic criteria for AKI-HRS [76]. In the course of medical development, people have been looking for new biomarkers to distinguish between patients with cirrhosis and other kidney diseases caused by AKI. These biomarkers included N-acetyl-B-D-glucosaminidase (NGAL), up-regulated tubular protein up regulated by injury, and plasma protein with diminished tubular reabsorption [77,78]. Of these indicators, NGAL has been the most widely studied biomarker for patients with cirrhosis.When patients with cirrhosis develop ascites and there are diagnostic criteria for acute kidney injury caused by hepatorenal syndrome, a series of clinical manifestations of nervous and psychiatric systems appear, and uremic encephalopathy caused by HRS can be clinically diagnosed after excluding structural kidney injury.

Treatment and Prevention

UE is mainly due to the further deterioration of the disease caused by a series of inducement on the basis of uremia, hyponatremia, Infection, increased plasma renin activity, liver reserve function and ascites severity are all predictors of acute kidney injury

caused by hepatorenal syndrom [79,80]. Acute hemodynamic changes associated with infection and extensive puncture drainage without albumin injection are the most common causes of AKI-HRS [63]. A study has shown that long-term use of albumin not only reduces the incidence of hepatorenal syndrome but also improves overall surial in patients with decompensated cirrhosis and ascites [81]. This suggests that another benefit of albumin is that it has important antioxidant and anticoagulant properties and helps stabilize vascular endothelial function [82]. For patients at risk for spontaneous bacterial peritonitis, prevention based on low ascites albumin with hepatic or renal dysfunction can not only prevent the occurrence of spontaneous bacterial peritonitis, but also significantly reduce the risk and the overall mortality of AKI-HRS [83,84].

The latest diagnostic criteria eliminate the minimum serum creatinine concentration, which allows for earlier diagnosis and treatment of AKI-HRS. This may lead to higher reversal rates and better treatment outcomes. Once the diagnosis of AKI-HRS is established, intravenous infusion of albumin 1g/kg/d for 2days should be initiated and diuretics should be discontinued [85].

Specific treatment of AKI-HRS includes vasoconstrictor agents combined with albumin infusion and reversal of acute variation factors. Multiple randomized controlled trials have confirmed the efficacy of angiotensin, which represents the main therapy for AKI-HRS [86]. Effective arterial blood volume (EABV) and renal blood flow are increased, especially when combined with venous albumin infusion, due to reduced portal venous pressure in cirrhotic patients.

Hemodialysis combined with blood perfusion plays an irreplaceable role in the treatment of UE caused by hepatorenal syndrome. It is mostly caused by the accumulation of toxic substances in plasma. Currently, there are no specific drug for clinical treatment. Hemodialysis combined with blood perfusion is a treatment method that can remove excessive toxic substances deposited in blood to achieve the purpose of purifying blood. The types of poison removed by different filtration methods are different, and the specific treatment outcomes are also very different. Some studies suggest that uremia patients already have abnormal coagulation function, and hemodialysis may damage the endothelial cell function of patients, thereby increasing the risk of bleeding or thrombosis. Hemodialysis combined with blood perfusion can not only effectively remove water-soluble small molecule poisons, but also remove protein-binding poisons and molecular poisons, so as to improve vascular endothelial function and promote coagulation function to return to normal. It has gradually become one of the first clinical treatment methods for uremic encephalopathy.

Transjugular intrahepatic portal shunt (TIPS) is also one of the combined hepatorenal treatment methods to reduce portal pressure. TIPS has shown significant benefit in patients with cirrhosis who cannot tolerate diuretics or refractory ascites and who cannot control variceal bleeding [87,88]. One study showed a significant improvement in renal function and a decrease in plasma renin activity, aldosterone, and norepinephrine concentrations after TIPS placement in AKI-HRS [89]. But with respect to general HRS patient, its condition is severe, liver function is poor, cannot tolerate operation, so the applications are relatively less.

Kidney transplantation therapy may be appropriate for patients with AKI-HRS who have not responded to medical therapy and are associated with volume overload, uremia, or electrolyte disturbances. Studies have shown that kidney transplantation does not reduce mortality from hepatorenal syndrome [90]. It is mainly used for pretransplant support in patients who wish to undergo liver transplantation [91].

At present, liver transplantation is considered to be the best method for the treatment of AKI-HRS. Hepatorenal syndrome is a serious liver cirrhosis that leads to systemic hemodynamic disorders and ultimately causes functional kidney damage. Therefore, liver transplantation can eliminate a series of abnormal liver function and portal hypertension brought by cirrhosis, so that renal function can be restored [92,93]. However, kidney injury is often caused by multiple factors, and patients may still have progressive decline in renal function or even death after liver transplantation. Therefore, when conditions are available, liver and kidney transplantation can be carried out simultaneously, but there are problems such as lacks of donors and difficulty in eliminating the difference between donors and ligands.

Dysglycemic Encephalopathy

Glucose is the most important energy substance and the basis of human metabolism. In a healthy person, the concentration of blood sugar is always maintained at a relatively stable level. In fasting state, blood glucose is between 3.9 mmol/l and 6.1 mmol/l. Blood sugar is the most important energy source for the central nervous system, and it can only be transported to the brain from other parts of the body, so maintaining optimal blood sugar levels is critical for survival [94]. When diseases occur in the human body, such as hepatobiliary and pancreatic diseases, after surgical treatment, the human body cannot obtain enough glucose from the outside in a normal way, and it needs to be supplemented iatrogenic.When the human body supplements nutrients through total parenteral nutrition (TPN), the blood sugar level of the body often has a large fluctuation, thus showing different severity of clinical symptoms. When there is low blood glucose occurs, it is manifested as peripheral nerve or cerebral nerve palsy, cold skin, convulsion, coma, and damp etc [95]. When blood sugar is too high, it is manifested as delirium, coma, partial hemichorea and throwing movement [96]. In actual clinical cases after surgery, brain dysfunction caused by blood glucose disorder is not difficult to find. However, due to the underlying diseases and surgical trauma of patients, it is often difficult to further identify brain dysfunction caused by blood glucose disorder after monitoring patients' blood glucose.In clinical work, doctors should timely adjust the clinical nutritional support program of patients after surgery. During TPN, patients' blood glucose fluctuations were monitored in a timely

manner, and the proportion of exogenous insulin and high sugar concentration was appropriately allocated to ensure that patients' blood glucose concentration remained in a relatively stable state.

Pathophysiology

Glucose is the most important substrate of the brain. Under normal conditions, the glucose concentration in the brain is close to 25%-30% of the blood circulating level, so it is highly dependent on plasma concentration [97]. The glucose requirement of normal brain is about 5 mg per minute per 100g brain tissue.The blood glucose disorder occurs in the form of hyperglycemia, hypoglycemia and/or significant blood glucose fluctuations, regardless of whether the patient has diabetes in the past or not [98]. Hyperglycemia can lead to brain damage in human body through a variety of mechanisms, resulting in corresponding clinical symptoms. In acute brain injury, glucose transporters in neurons and astrocytes are up-regulated by increasing regulators, resulting in a large amount of passive glucose transport to brain tissue [99]. When the blood-brain barrier is destroyed, neuronal glucose overload may lead to excessive oxidative stress through the over activation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, thus producing living oxide [100]. Studies have shown that both hyperglycemia and hypoglycemia, as well as significant fluctuations in blood glucose, will affect the function and activity of neurons, leading to apoptosis of astrocytes, activation of microglia, and even damage and apoptosis of neurons. During this process, oxidative stress and inflammatory response increase, which may also lead to glucose reperfusion injury Mitochondrial dysfunction and anaerobic glycolysis [101]. Transient hypoglycemia deprives the brain of its main energy. Both the effect of hypoglycemia on brain tissue and the subsequent glucose reperfusion injury may cause damage to brain tissue [102]. Clinical studies have shown that fluctuations in blood glucose levels are the cause of independent cognitive impairment [103]. The ratio of glycosylated hemoglobin/HbA1 is a sign of the fluctuation of blood glucose level, which has been proved to be an independent factor, leading to the decline of cognitive function in elderly people with diabetes [104].

Manifestations and Diagnosis

In actual clinical work, patients' blood sugar fluctuations are often changeable, and the clinical symptoms are different in severity, but most of them are in two forms, namely, when blood sugar is too low, it is manifested as peripheral nerve or cerebral nerve paralysis, skin wet and cold, twitching, coma, and other hypoglycemic systemic reactions [95]; Hypertonic hyperglycemia syndrome and ketoacidosis may occur in patients with hyperglycemia, but these two hyperglycemic crises are not common in actual clinical work, mainly manifested as insanity, delirium, coma, hemichorea and throwing movements [96]. Under normal circumstances, the fasting circulating blood glucose level of adults is between 4.4 mmol/l and 6.1 mmol/l. Initially, a decrease in blood sugar levels activates the defense against hypoglycemia. First, when the blood sugar level falls below the lower normal limit, insulin secretion decreases. Below 3.8 mmol/l, glucagon secreted by pancreatic b cells and adrenaline secreted by adrenal medulla increased. If the above mechanisms cannot stop the hypoglycemia attack, a lower blood glucose level (below 3.5 mmol/l) will lead to autonomic nervous symptoms, including anxiety, tachycardia, sweating and mydriasis. These symptoms usually promote behavioral defense and food intake. If the blood sugar drops below 2.8-3.0 mmol/l, there will be neurological hypoglycemic symptoms, such as confusion or seizures. When the blood glucose level is lower than 2.3-2.7 mmol/l, coma may occur. Hypoglycemic brain injury is different from cerebral ischemia in the neuropathological distribution [105]. The operation process of blood glucose detection is not rechecked, and the patient's blood glucose can usually be known immediately. However, for newly admitted patients, we need to know about their previous blood sugar through other detection methods, especially for patients with diabetes. HbA1c can reflect the average blood sugar level of patients for 2-3 months, which is a very valuable indicator for judging the blood sugar control of patients. Generally, the HbA1c of normal people is below 6.5 mmol/l, while for diabetic patients, it is usually required to be controlled below 7%. By detecting the fasting blood glucose, blood glucose two hours after meal and HbA1c, we can generally understand the blood glucose level of the patient well, so as to judge the hypoglycemia or hyperglycemia of the patient.

Treatment and Prevention

Mild hypoglycemic events can be treated by taking fast absorbed carbohydrate and glucose tablets orally. Generally, nutrition absorption and plasma glucose are allowed to return to the normal level within 15 minutes, and blood glucose is measured again after 15 minutes (Table 5) [106-109]. In one study, patients with hypoglycemia accompanied by mental decline were given 10% or 25% glucose solution, 50 ml at a time, and repeated every 1minute until the patients regained consciousness or were given the maximum dose of 25g [110]. The results showed that the median total dose required for receiving 10% glucose solution was 10g, while 25g was required for receiving 25% glucose solution. In order to prevent the occurrence of hypoglycemia, for patients who have used insulin therapy, continuous subcutaneous injection of insulin, alone or in combination with continuous glucose monitoring devices, can reduce the risk of hypoglycemia [111]. For patients undergoing hypoglycemic treatment, the blood glucose target has been revised from 4.4-6.1 mmol/l recommended earlier to 5.5-10.0 mmol/l. This range minimizes the risk of hypoglycemia.When the blood glucose level drops to<5.5 mmol/l, it is recommended to modify the hypoglycemic drugs. The body weight based insulin administration strategy uses 0.4- 0.5U/kg/day as the total daily dose, or 0.20-0.25 U/kg/day as the basic insulin regime [112,113]. For patients with hypertonic hyperglycemia syndrome and ketoacidosis, timely detection and active treatment should be carried out. The key to treatment is to supplement the lost liquid. 1000-2000 ml 0.9% NaCl should be infused intravenously within 1-2 hours to quickly restore blood pressure. According to the serum sodium concentration, 0.9% physiological saline or 0.45% saline was infused at the rate of 250-500 ml/h. When the plasma glucose level reaches around 11.1 mmol, it is changed to glucose plus 5% saline. Routine insulin was injected intravenously at 0.1U/kg, and then insulin was continuously infused at 0.1 U/kg/h. When glucose≤13.9mmol/l, the insulin rate was reduced to

0.05U/kg/h.Thereafter, the regulation rate maintained the blood glucose level of about 11.1 mmol/l [114-116]. At the same time, monitoring the concentration of serum potassium and bicarbonate is also crucial, and it should also be adjusted in real time according to the detection results. For the prevention of these two kinds of acute and critical diseases, patients should be instructed how to adjust the insulin dosage during the disease, and it is important to insist on not stopping insulin, visit the specialist on time, and strictly follow the doctor's advice to control blood sugar. In the actual clinical cases after surgery, it is not difficult to find the brain dysfunction caused by blood glucose disorder. However, due to the underlying disease and surgical trauma of the patient, after we have monitored the blood glucose of the patient, it is often difficult to further understand the brain dysfunction caused by blood glucose disorder.Therefore, when preparing for surgery, the patient's blood sugar should be carefully inquired or monitored. If necessary, the patient's HbA1c should be checked to understand the patient's recent blood sugar. In patients undergoing surgery, In particular, patients undergoing pancreatectomy do not have the function to regulate blood sugar normally, and under the condition of enteral nutrition and/or total parenteral nutrition for nutritional support, blood sugar disorder is likely to occur. Therefore, we should not only monitor the blood sugar of patients in a timely manner, but also reasonably allocate the ratio of exogenous insulin to high concentration glucose, and reasonably add amino acids and fat emulsion to ensure that the blood sugar concentration of patients remains relatively stable while receiving adequate nutritional support.

Intravenous fluids 1000-2000 ml 0.9% NaCl over 1-2 h for prompt recovery of hypotension and/or hypoperfusion. Switch to 0.9% saline or 0.45% saline at 250-500 ml/h depending upon serum sodium concentration. When plasma glucose level~11.1 mmol, change to dextrose in 5% saline. **Insulin** Regular human insulin intravenous bolus of 0.1 U/kg followed by continuous insulin infusion at 0.1 U/kg/h. When glucose level ≤13.9mmol/l, reduce insulin rate to 0.05 U/kg/h. Thereafter, adjust rate to maintain glucose level ~11.1 mmol/l. Subcutaneous rapid-acting insulin analogues might be an alternative to intravenous insulin in patients with mild-to-moderate DKA. **Potassium** Serum potassium level >5.0 mmol/l (no supplement is required); 4-5 mmol/l (add 20mmol potassium chloride to replacement fluid); 3-4 mmol/l (add 40 mmol to replacement fluid); <3 mmol/l (add 10-20 mmol/h per hour until serum potassium level>3 mmol/l, then add 40 mmol to replacement fluid). **Bicarbonate** Not routinely recommended. If pH <6.9, consider 50 mmol/l in 500 ml of 0.45% saline over 1h until pH increases to ≥7.0. Do not give bicarbonate if pH ≥7.0. **Laboratory evaluation** lnitial evaluation should include blood count; plasma glucose; serum electrolytes, ureanitrogen, creatinine, serum or urine ketone bodies, osmolality; venous or arterial pH; and urinalysis. During therapy, measure capillary glucose every 1-2 h. Measure serum electrolytes, blood glucose, urea nitrogen, creatinine and venous pH every 4 h. **Transition to subcutaneous insulin** Continue insulin infusion until resolution of ketoacidosis. To prevent recurrence of ketoacidosis or rebound hyperglycaemia, continue intravenous insulin for 2-4 h after subcutaneous insulin is given. For patients treated with insulin before admission, restart previous insulin regimen and adjust dosage as needed. For patients with newly diagnosed diabetes mellitus, start total daily insulin dose at 0.6 U/kg/day. Consider multi-dose insulin given as basal and prandial regimen.

Table 5: Treatment of hyperglycaemic crises.

Conclusion

The etiology of metabolic encephalopathy is various. Since its clinical manifestations are similar neuro-psychiatric symptoms, with no specificity. The examination methods of metabolic encephalopathy are relatively reexamined, so it is difficult for clinicians to make a clear diagnosis of its etiology. In patients with hepatobiliary and pancreatic diseases requiring surgical treatment, careful examination and evaluation should be carried out before surgery. To find out the predisposing factors and potential causes of metabolic encephalopathy as much as possible and actively correct it, because prevention and treatment are equally important. When it is suspected that a patient has developed metabolic encephalopathy, it is necessary to start treatment according to the possible etiology of it while performing relevant examinations and contacting a neurologist for diagnosis and treatment, rather than waiting until the disease is clearly diagnosed, because when the disease is diagnosed, it may also aggregated.

Statements and Declarations

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Competing Interests

The authors declare that they have no conflict interests.

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Ethics

This artical does not involve medical ethics.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article.

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