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Hepatorrenal syndrome: up ToDate

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Abstract

Hepatorenal syndrome (HRS) is a frequent and severe complication in patients with hepatic cirrhosis and portal hypertension and is characterized by circulatory abnormalities leading to renal vasoconstriction, generating functional renal failure.

Its pathophysiology has been studied and the prognosis is reserved unless the patient receives a liver transplant.

Drug therapy with splenic vasoconstrictors is the future hope of these patients while they undergo liver transplantation.

Key words: Hepatorenal syndrome, Renal insufficiency, Liver cirrhosis, Treatment.

Síndrome hepatorrenal: Revisión de la literatura

Resumen

El síndrome hepatorrenal (SHR) es una complicación frecuente y severa en pacientes con cirrosis hepática e hipertensión portal y se caracteriza por anormalidades circulatorias que llevan a vasoconstricción renal, generando insuficiencia renal funcional.

Su fisiopatología ha sido estudiada y el pronóstico es reservado a menos que el paciente reciba trasplante hepático.

El tratamiento medicamentoso con vasoconstrictores esplénicos es la esperanza futura de estos pacientes mientras acceden a trasplante hepático.

Palabras clave: Síndrome hepatorrenal, Insuficiencia renal, Cirrosis hepática, Tratamiento.

Introduction

Hepatorenal syndrome (HRS) is a potentially reversible pathology that occurs in patients with chronic cirrhotic liver disease, as well as in patients with acute liver failure. It is characterized by an intense renal vasoconstriction that leads to a decrease in renal percussion and glomerular filtration rate[1]. Studies of renal histology in these patients are normal or show minimal abnormalities that do not explain the deterioration of renal function, because this is considered a type of "functional" renal failure in cirrhotic patients and is the most common cause of azotemia in this group of patients[2].

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The functional nature of this type of renal failure has been reinforced by the absence of alterations in the histology of the compromised kidneys by studies showing that the kidneys of cirrhotic patients with HRS regain normal renal function when they were transplanted to patients with renal insufficiency Terminal, without liver disease or that the HRS is reversible after liver transplantation and, finally, the reversibility of HRS with pharmacological treatment. We will review the pathophysiology, diagnosis, clinical and treatment of this pathology.

PHYSIOPATHOLOGY

For several years HRS was considered associated with 2 main problems: irreversible terminal liver failure and functional renal failure secondary to renal vasoconstriction; The majority of investigators considered that the relationship between the two types of failure: renal and hepatic, was secondary to a systemic hemodynamic deterioration associated to arterial vasodilation in the splenic tree. However, during the last decade a body of scientific evidence suggests a complex syndrome that affects much more than only 2 organs, suggesting that the deterioration of systemic circulatory function associated with HRS not only affects the kidney but also compromises other regional circulations[2].

Four concepts have emerged with the accumulation of research[3]:

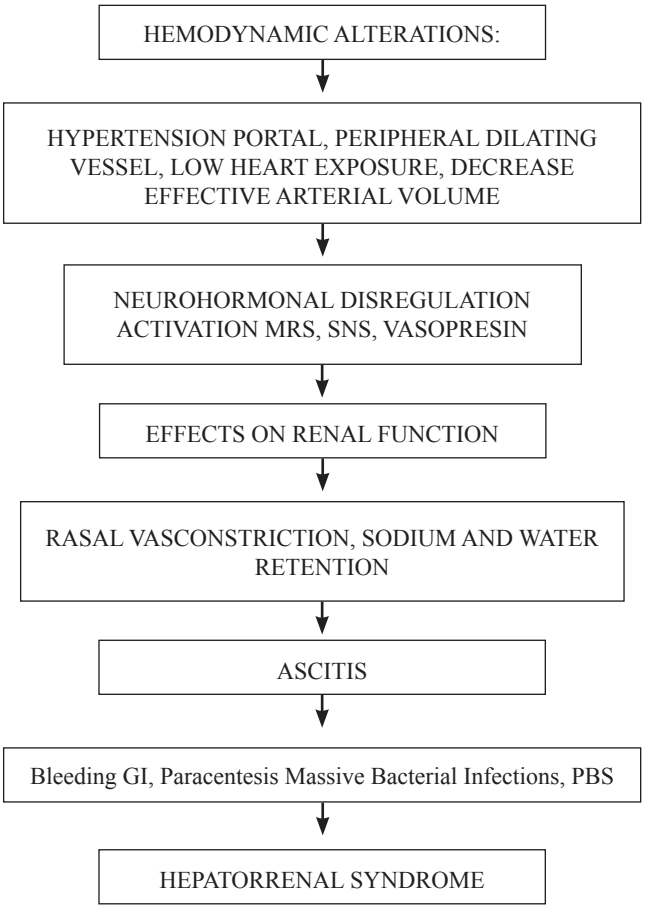
1. Extrarenal arterial vasodilatation occurs mainly at the level of the splenic tree, whereas in other vascular trees, the opposite occurs, vasoconstriction, as in the case of the kidney, liver and brain, which will contribute to the development of encephalopathy, Hepatic and renal failure.
2. Cardiac output in patients with HRS may be diminished and insufficient to respond to the needs of the individual.
3. Spontaneous bacterial peritonitis (SBP) is the most frequent precipitating event of HRS type 1.
4. Pharmacological treatment can reverse HRS and improve survival in this group of patients.

Vasodilatation of the splenic tree is mainly caused by the presence of nitric oxide and other vasodilatory substances[4]. Early in the course of the disease, the decrease in systemic vascular resistance is compensated by the development of hyperdynamic circulation (increased heart rate and cardiac output), however, as the disease progresses and arterial vasodilation increases, The hyperdynamic circulation is insufficient to correct effective arterial hypovolemia. The resulting hypotension leads to the activation of compensatory mechanisms: renin angiotensin system (RAS), autonomic nervous system (ANS) and antidiuretic hormone, leading to a retention of water, sodium and, subsequently, to the formation of ascites and dilutional hyponatremia. In this advanced stage of disease, RAS and ANS are markedly stimulated and blood pressure is critically dependent on the effect of these systems on vascular tone.

Because the splenic tree is resistant to the vasoconstriction of these compensatory mechanisms (mediated by angiotensin II, norepinephrine, vasopressin and endothelins) by the local release of nitric oxide and other vasodilator substances, the maintenance of blood pressure is based on the vasoconstriction of extra-splenic vascular territories such as the kidney and brain. HRS develops in the last phase of the disease (of which disease is cirrhosis, ascites or renal failure?), when there is deterioration in the effective arterial volume and severe hypotension[6]. The intense vasoconstriction generated leads to a marked decrease in renal perfusion, azoemia and increase in serum creatinine (Crs). Therefore, renal vasoconstriction in HRS is the consequence of a simultaneous effect of numerous vasoactive mechanisms on the intrarenal circulation[7]. The second concept is that the reduction of cardiac output in HRS patients leads to renal hypoperfusion. The different studies performed in patients with HRS with refractory ascites show that cardiac output is significantly reduced compared to patients without HRS.

The mechanism of low cardiac output in HRS is unknown. Cardiac abnormalities are characterized by an attenuated systolic and diastolic response to the stimulus, changes in repolarization and hypertro-

Figure 1. Pathogenic mechanisms of the HRS



phy of the cardiac cavities, a situation that has been termed as cirrhotic cardiomyopathy. A decrease in preload secondary to a decrease in venous return is one of the hypotheses.

HRS may develop spontaneously during the course of the disease, but also occurs by precipitating events. The most frequent and important ones are infections such as spontaneous bacterial peritonitis, gastrointestinal bleeding and large volume paracentesis without adequate replacement of albumin[9].

Diagnosis and epidemiological aspects

It should be borne in mind that for any definition of deterioration of renal function or acute renal injury in any pathology, including liver diseases such as cirrhosis or hepatic impairment, measurement of Crs remains the most practical and widely accepted method for the estimation of renal function in clinical practice, and is the basis of existing definitions of acute kidney injury (AKI). The prognostic impact of renal function on liver disease is reflected in the inclusion of Crs in the model for the end-stage score of liver disease (MELD), which is used to prioritize patients for liver transplantation[10]. However, in cirrhosis, Crs is notoriously inaccurate in the diagnosis of renal dysfunction, since it overestimates renal function due to decreased creatinine production due to caloric malnutrition, liver, protein and loss of muscle mass[10-13]. In addition, measurement of Crs using the Jaffe method can be artificially lowered due to hyperbilirubinemia13, or by use of cephalosporins[14] leads to variability in MELD[15] scores.

Cystatin C has been suggested as a sensitive marker of renal function[16-22]. However, recent studies have shown that, like creatinine, cystatin C is affected by age, sex, muscle mass and liver disease and overestimates renal function in patients with cirrhosis[17-29]. In conclusion the measurement of Crs should be used to assess renal function in patients with advanced cirrhosis until more reliable methods of measuring renal function are generalized[29].

HRS is defined as renal failure occurring in patients with acute or chronic liver disease with portal hypertension, in the absence of laboratory and anatomical evidence of other known causes of renal failure.

The annual incidence of HRS in patients with cirrhosis and ascites has been estimated at 8%. The annual probability of developing HRS in cirrhotic patients is estimated at 18% at 1 year and at 39% at 5 years. Due to the functional nature of renal failure there is no specific marker of HRS[11,20]. HRS is the complication associated with cirrhosis with worse prognosis and is considered as the terminal event of the disease.

Although HRS is the most common cause of azoemia in patients with advanced cirrhosis, other causes of renal failure should be ruled out in these patients. Therefore, the first step in the management of cirrhotic patients with impaired renal function or oliguria is a correct diagnosis of the etiology of renal impairment.

As there is unfortunately no specific test to make a conclusive diagnosis of HRS, its adequate diagnosis

is based on the exclusion of other types of renal failure that may occur in this group of patients, therefore HRS is a diagnosis of exclusion[35].

Two basic aspects should be taken into account when making this diagnosis: the first is the reduction of the glomerular filtration rate and the second is to differentiate HRS from other causes of renal failure.

Regarding the first point, it should be taken into account that the muscle mass and, therefore, the creatinine release is considerably reduced in this group of patients, reason why the cirrhotic patients can have creatinine in normal range with a rat of markedly decreased glomerular filtration. Also urea, which is synthesized by the liver, is reduced as a result of liver failure.

Due to the lack of specificity of markers for HRS, in 1996 the first diagnostic criteria of HRS, proposed by the International Ascites Club, were published and were based on the 3 main concepts of the time:

1. Renal failure in HRS is functional and caused by severe renal arteriolar vasoconstriction.
2. HRS occurs in patients with systemic circulatory dysfunction caused by extrarenal vasodilation.
3. Volume expansion does not improve renal function.

However, due to a better understanding of the pathogenesis of HRS and the introduction of new therapeutic tools, the need arose to rethink its definition and establish new criteria for the International Ascites Club in 2007.

The main differences with the 1996 criteria are:

1. The potential reversibility of HRS even without hepatic transplantation.
2. The dominant role of arterial vasodilation in the splenic tree.
3. The frequent role of spontaneous bacterial peritonitis as a precipitating factor in HRS type 1.

The criteria established by the International Ascites Club 2007 for HRS are:

The main differences between the 2 diagnostic criteria (old and new) are:

A. To. Exclusion of 24-hour creatinine clearance because it is more complicated than Crs for routine purposes and does not increase accuracy in estimating renal function in cirrhotic patients.

B. Functional renal failure may occur at the site of an infectious bacterial process, but in the absence of septic shock. This means that HRS treatment can be started without waiting for recovery of renal function to be completed

C. The volume expansion should be with albumin rather than saline, because the former causes a better and more sustained expansion.

D. The smaller criteria were excluded as the expert panel concluded that they are not essential.

Table 1. Diagnostic criteria for hepatorenal syndrome proposed by the International Ascites Club, 1994

Major Criteria:
1. Presence of acute or chronic liver disease with hepatic failure and portal hypertension.
2. Absence of shock, volume depletion, ongoing infectious process, nephrotoxic drugs.
3. Decreased filtration rate as a Crs greater than 1.5 mg / dl or a 24-hour creatinine clearance less than 40 ml / min.
4. No improvement in renal function (decrease in Crs to values below 1.5 mg / dl or an increase in creatinine clearance in 24 hours greater than 40 ml / min) after discontinuation of diuretics and Expansion of the plasma volume with 1.5 l. Of plasma volume expanders.
5. Proteinuria less than 500 mg / day and absence of obstructive uropathy or parenchymal renal disease by ultrasound.
Minor Criteria:
1. Urinary volume <500 ml / day.
2. Urinary sodium <10 meq / l.
3. Urinary osmolality greater than plasma.
4. Red blood cells in urine under 50 per high power field.
5. Serum sodium concentration less than 130 meq / l.

Source: Arroyo V, Ginés P, Gerbes A, et al. Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. Hepatology 1996; 23: 164-176[35].

Recently, the eighth international consensus conference of the Acute Dialysis Quality Initiative Group (ADQI) proposed what it called renal disorders or dysfunctions associated with cirrhosis. The final consensus of the working group proposed to apply the RIFLE criteria to define AKI in patients with cirrhosis, regardless of whether the cause of acute deterioration of renal function was related to a functional or structural disorder[47]. (Table 2).

Clinic of hepatorenal syndrome

When faced with a patient with liver disease and with impaired renal function, we must think of 3 possibilities, which are the most frequent in this type of patients: HRS, prerenal azotemia and acute tubular necrosis, not to say with this That we should not think of other causes of renal failure that are less frequent[15].

Two types of HRS7 are clinically known:

HRS type 1 is characterized by a severe and rapid progressive renal failure, defined by the dubbing of Crs, reaching a level higher than 2.5 mg / dl in less than 2 weeks. Type 1 HRS may appear spontaneously during the course of the disease, but the most common is that it is related to a precipitating event, the most frequent being a spontaneous bacterial peritonitis (SPB) -like infectious process followed by gastrointestinal tract bleeding, Surgery or an acute hepatitis on a cirrhosis. Patients with SPB develop HRS by 25%. Without treatment the HRS type 1 implies a poor prognosis and a survival of approximately 2 weeks after the onset of renal failure.

Table 2. The criteria established by the International Ascites Club 2007 for HRS are:

1. Cirrhosis with ascites.
2. Crs> 1.5 mg / dl (> 133 umol / l).
3. No improvement in Crs (decrease to <133 umol / l) after 2 days of diuretic suspension and volume expansion with albumin. The recommended dose of albumin is 1 g / kg / day, to a maximum of 100 g / day.
4. No shock.
5. Current or recent absence of nephrotoxic drugs.
6. Absence of renal parenchymal disease suggested by the presence of proteinuria> 500 mg / day, hematuria (> 50 red cells per high power field), or renal abnormalities by ultrasonography[36].

Source: Gut 2007; 56; 1310-1318.

The HRS type 2:

It is characterized by renal failure that is not established rapidly and a reduction in renal function (Crs from 1.5 to 2.5 mg / dl) occurring for weeks or months. It may also appear spontaneously or by a precipitating event, but is usually associated with refractory ascites. The survival of this group of patients is better (4-6 months) than that of patients with HRS type 1, but worse than that of non-azoemic cirrhotic patients with ascites.

Treatment

Although HRS is the most common cause of azoemia in patients with advanced cirrhosis, other types of renal failure should be ruled out. Therefore, the first step in the management of patients with acute or chronic liver disease with renal failure is the correct diagnosis of the etiology of the deterioration of their renal function8.

Prevention of HRS

If it is accepted that there are known situations that can precipitate HRS such as: infections, especially spontaneous bacterial peritonitis, hypovolemia induced by digestive bleeding or paracentesis of large volumes without albumin replacement; The prevention must start from the adequate knowledge and treatment of these situations.

Randomized controlled trials have been published in which SHS can be prevented in special clinical situations:

1. The incidence of HRS in patients with PBS may be reduced by the administration of albumin. At

Table 3. The Quality Initiative for Acute Dialysis (ADQI) criteria for the Definition and classification of acute renal injury (modified criteria RIFLE)37http://ccforum.com/content/16/1/R23 - B41.

AKI Stage	Serum creatinine criteria	Urine output criteria
1 (Risk)	Increase Scr ≥ 0.3 mg / dl within 48 hours or a 150-200% (1.5-2 fold) increase in baseline	<0.5 ml / kg / hour for> 6 hours
2 (injury)	Increase Scr 200% to 299% (≥ 2 to 3 times) from the start	<0.5 ml / kg / hour for> 12 hours
3 (FAILURE)	Increase Scr ≥300% (≥ 3 times) from onset or Scr ≥4.0 mg / dl with an acute increase of ≥0.5 mg / dl or initiation of renal replacement therapy	<0.3 ml / kg / hour for 24 hours or anuria for 12 hours

SCR = Serum creatinine

Table 4. Proposed diagnostic criteria for renal dysfunction in cirrhosis[47]

Diagnosis	Definition
Acute kidney injury	• An increase of Scr ≥50% of the initial value or an increase Scr> 0.3 mg / dl • Type-1 HRS is a specific form of acute kidney injury
Chronic Kidney Disease	• GFR <60 ml / min for> 3 months calculated according to MDRD-6 formula
Acute RI in chronic	• Increased Scr ≥50% of baseline or an increase of Scr> 0.3 mg / dl in a patient with cirrhosis who had GFR <60 ml / min for> 3 months calculated according to MDRD-6 formula

GFR, glomerular filtration rate; HRS, hepatorenal syndrome; Scr, serum creatinine. Both acute deterioration of renal function and chronic renal dysfunction fundus may be functional or structural in nature. MDRD-6: TFG = 170 × Scr (mg / dL) -0.999 x age -0.176 x 1.180 (if black) × 0.762 (if female) × serum urea nitrogen -0,170 × albumin 0.138

the time of diagnosis of PBS, in addition to antibiotic treatment, albumin is recommended with an initial dose, the first day of 1.5 g / kg body weight and 1 g / kg per day, to a maximum dose of 100 and 150 g, Respectively. Albumin infusion has been shown to reduce the incidence of HRS type 1 and reduced mortality (10% incidence of HRS type 1 in the albumin group vs. 33% in the control group and mortality in 22% albumin group vs. 41 % Control group) [12].

2. Preventing the onset of PBS. Primary prophylaxis of PBS in high-risk patients using quinolones is associated with a significant decrease in the development of PBS and HRS type 1, as well as an increase in survival of 3 and 12 months.

Therefore, prophylaxis is recommended in cirrhotic patients with ascites with gastrointestinal bleeding; Short-term (7-day) administration of norfloxacin 400 mg every 12 hours is suggested. Long-term antibiotic use (oral norfloxacin 400 mg / day) is recommended in patients who have had previous episodes of PBS58. ((References 48 to 57 are missing))

Treatment options in HRS:

1. Pharmacological treatment:

Treatment with vasoconstrictors and albumin is the treatment of choice for HRS type 134. The goal of treatment is to produce vasoconstriction in the splenic vascular bed as well as to reduce effective hypovolemia.

The study of the pathophysiology of HRS and based, above all, on the arterial vasodilatation of the splenic tree, have led the different researchers to study and use vasoconstricting drugs of the splenic circulation, in order to reverse pharmacologically and in a more Physiological the circulatory dysfunction of HRS and thus improve renal function.

The first drug used for this purpose was dopamine, however, subsequent studies showed that the administration of dopamine in cirrhotic patients with ascites, with and without HRS has little effect on re-

Table 5. Differential diagnosis of acute renal failure in cirrhotic patients

	HRS	Prerenal	Acute Tub Nec
Urinary Sedi	Normal	Cilin hyalinos	Cilin Granular / epithelial cells
FENA	<1	<1	>2
NA urinary	<10	<20	>40
OSM urinary	Variable	>500	<300
Specific dens	>1.2	>1.20	~1.010
Creat ratio U/P	>40:1	>40:1	<20:1
Resp to plasma expanders	Bad	Good	Variable

nal function. Since then, numerous vasoconstrictors have been studied.

To date, 3 types of vasoconstricting agents have been used in the treatment of HRS[56]:

to. Somatostatin analogues: octreotide

B. Vasopressin analogs: ornipresin, terlipressin

C. Alpha adrenergic agonists: norepinephrine, midrodine

Ornipresin and terlipressin are the vasopressin analogues that have been used in HRS; however, ornipressin despite the benefit shown in the reversal of HRS has been abandoned because of its ischemic effects: cardiac arrhythmias, myocardial ischemia, cutaneous necrosis .

Terlipressin or triglycerolysine vasopressin is a synthetic derivative of vasopressin that has a dominant action on V 1 receptors, which explains its potent vasoconstrictor effect; Its plasma half-life is longer (4-10 hours) than that of other analogues, which facilitates its administration in intravenous boluses rather than continuous infusion. To date it is the most extensively studied vasoconstrictor, used in HRS type 1 and available in our country.

The starting dose is 1 mg every 4-6 hours. If there is no response (Crs decrease by 25% after 2 days), the dose may be folded every 2 days up to a maximum of 12 mg / day. The treatment can be discontinued if the Crs does not decrease by 50% after 7 days of being at the maximum dose or if there is no reduction after 3 days. In patients with early response, treatment should be continued until the reversal of HRS or for a maximum of 14 days or by the presence of ischemic side effects and arrhythmias induced by terlipressin.

Table 6. Vasoconstrictor drugs for the treatment of hepatorenal syndrome

Drugs	Dose
Terlipressin 60-78	0.5 to 2.0 mg intravenously every 4 to 6 hours; With gradual increases in dose every few days if there is no improvement in Crs, up to a maximum dose of 12 mg / day, as long as there are no side effects. Maximum treatment 14 days
Vasopressin81	0.01 U / min at 0.8 U / min (continuous infusion). Rate to achieve a 10 mmHg increase in MAP baseline or MAP> 70 mmHg
Noradrenaline[69,77,80]	0.5 to 3.0 mg / hour (continuous infusion). Assess for an increase of 10 mmHg in MAP
Midodrine + octreotide[82-87]	Midodrine: 7.5 to 12.5 mg orally 3 times. Value to achieve a 15 mmHg increase in baseline MAP
	Octreotide: 100-200 mg subcutaneously 3 times daily or 25 mg bolus followed by intravenous infusion of 25 mg / hour

MAP: Mean arterial pressure

Source: Nadim et al. Critical Care 2012 16: R23 doi: 10.1186 / cc11188

Concomitant administration of albumin-like volume expanders may improve the effect of vasoconstrictors. The recommended dose of albumin is 1 g / kg

body weight as the initial dose, up to a maximum of 100 g and continue with 20-40 g / day.

With the use of terlipressin and albumin, up to 60% of HRSs can be reversed. Renal insufficiency may recur as much as 15% after discontinuation of treatment, but resumption of treatment is equally effective.

A widely available alternative in our institutions is norepinephrine at a dose of 0.5-3 mg IV / hour in continuous infusion, to achieve a blood pressure increase of 10 mmHG.

Midrodine, an oral drug, has been used in patients with HRS type 1 at a dose of 7.5 mg (maximal 12.5 mg), every 8 hours, plus octreotide 100 mg subcutaneously, every 8 hours, associated with volume expansion With albumin at a dose of 20-40 g IV / day[23].

Octreotide an octapeptide analogue of somatostatin with potent vasoconstrictive action on the splenic vasculature has been used in HRS at a dose of 100 ug SC every 8 hours up to a maximum dose of 200 ug SC every 8 hours[23,26].

To date there are no studies supporting the use of vasoconstrictors in HRS type 2.

2. Intrahepatic transjugular portosystemic shunts (TIPS)

The development of transjugular intrahepatic portocava shunt (TIPS in the Anglo-Saxon literature: Transjugular intrahepatic portocaval shunt) obviates the need for a major surgical procedure such as portocava shunt, however, insertion of a TIPS is not a Simple procedure and is not without complications. Unfortunately, there are no adequately controlled studies to assess its efficacy in HRS.

TIPS works as a portocava derivation and is expected to improve portal hypertension. Its insertion is associated with an increase in cardiac output and an expansion of central blood flow. The simultaneous effect on splenic and systemic circulation may represent the mechanism by which TIPS improves renal perfusion, glomerular filtration, and excretion of urinary sodium and water.

In general, TIPS in small studies have been shown to improve kidney function and eliminate ascites. Patients with HRS type 1 may improve survival, which has not been demonstrated in HRS type 2. It should not be used in patients with bilirubin> 5 mg / dl, bacterial infection, presence of hepatic encephalopathy or history of recurrent encephalopathy , Severe cardiac or pulmonary dysfunction, or a Child-Pugh score> 1131.

3. Renal or hepatic dialysis

Renal replacement therapy has been used in the management of patients with HRS. Intermittent hemodialysis (IHD), venovenous hemodiafiltration (CVVHDF), high volume hemofiltration and peritoneal dialysis (PD) have been used, although there is no controlled evidence to evaluate its effectiveness in this situation[60-67].

Systemic hypotension frequently causes IHD not to be feasible in this group of patients, just as the presence of ascites and peritonitis reduces the efficiency of PD. However, renal replacement therapy is used in many centers as a bridging therapy while hepatic transplantation leaves[64].

Because the major cause of death in hepatic failure and decompensated cirrhosis is cerebral edema, as a result of increased intracranial pressure and decreased cerebral perfusion pressure, CVVD or continuous venous haemofiltration (CVVHDF) have been recommended As renal replacement therapy in this type of patients. The continuous nature of the procedure together with the lack of abrupt changes in mean arterial pressure and intracranial pressure allows a better removal of uremic toxins as well as mediators of inflammation and better cardiovascular stability[65].

Several methods of extracorporeal liver support or hepatic dialysis are being used in patients with acute or chronic acute hepatic failure, such as HRS, with increased frequency as bridging therapy while liver transplantation is ongoing. The goal of bioartificial systems would theoretically be to completely replace liver function both in detoxification and in synthesis, however, the complexity of both functions to be carried out by the different systems used remains a challenge. Therefore, to use machines that only fulfill the function of detoxification known as hepa-

tic dialysis, which remove from the circulation soluble toxins bound to albumin and which are believed to play a primordial role in the pathophysiology of hepatic failure.The molecular absorbent recirculating system (MARS) is a variant of albumin dialysis developed by Gambro and introduced since 1999[62]. Prometheus is another hepatic dialysis option based on fractional plasma separation and developed by Fresenius. Small studies, support safety and efficacy with both types of therapy, both methods should be considered experimental until large controlled and randomized trials demonstrate survival benefit[65].

4. Liver transplantation:

It is the treatment of choice in both HRS type 1 and 2. However, the main problem of liver transplantation (LT) in HRS type 1 is its applicability. Unfortunately, the poor survival of patients with HRS, especially type 1 (days to weeks), poor availability of organs and the different administrative barriers of our Health System make the liver transplantation very unlikely in this type of patients[40].

LT is considered to be the ideal treatment for patients with terminal liver disease[40-42]. Many of these patients are admitted for various degrees of concomitant renal dysfunction, including HRS. The LT can reverse the HRS. Patients with HRS who undergo LT have more complications, longer hospital stay in ICU and higher in-hospital mortality than patients transplanted without HRS. Similarly, the long-term survival of patients transplanted with HRS is good, from 60% to 3 years, slightly lower than that of transplant patients without HRS (70-80% at 3 years).

Hemodynamic and neurohormonal abnormalities associated with HRS disappear one month after surgery and patients regain the ability to excrete sodium and water.

With an aggressive pre and post-transplant management, an excellent result can be achieved in HRS patients with LT. In this sense, the search for therapeutic methods other than LT to improve renal or hepatic function, either temporarily or permanently (even to reverse HRS), or as bridging therapy until hepatic transplant appears, can be beneficial[40].

Final recommendations for treatment:

HRS type 1:

The use of vasoconstrictors combined with albumin is considered the first-line therapy, in case of lack of response the use of TIPS can be attempted. Replacement treatments, either hepatic or renal, can also be used as bridging therapy while liver transplantation is performed.

In HRS type 2 there is no support for the use of vasoconstrictors. TIPS can be used to improve refractory ascites[67].

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Conflict of Interest

The author declares that he has no conflicts of interest related to the publication or the contents of this article.

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