www.biogenericpublishers.com

Article Type: Review Article

Received: 11/06/2020

Published: 19/06/2020

Open Access Journal of Biogeneric Science and Research
ISSN 2692-1081

DOI: *10.46718/JBGSR.2020.01.000029*

Acute Liver Failure

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Abstract

Acute liver failure (ALF); sudden onset hyperbilirubinemia, hepatic encephalopathy (HE), coagulopathy in individuals without any known liver disease. It is a clinical syndrome characterized by high morbidity and mortality. In diagnosis, the underlying etiological reason, the patient's age and the duration of the disease are important for clinical course and prognosis. The higher the onset rate of the disease in ALF; that is, the shorter the time of development of encephalopathy, the greater the chances of patients recovering spontaneously. No reason can be found at a rate of 19%. In our country, hepatitis viruses are in the first place, drugs and toxins are in the second place. Liver transplantation is the most important and modern treatment method with proven efficacy. Uncontrolled sepsis, severe respiratory insufficiency, excessive inotropic agent requirement, metastatic cancer, active alcoholism, drug addiction and psychosocial causes are contraindicated for transplantation. The most drugs and herbal products are caused hepatotoxicity. Acetaminophen is the most common agent causing liver damage. If used as an antidote in acetaminophen toxicity in the early period, it effectively prevents the hepatotoxicity and ALF caused by the toxic metabolite of acetaminophen, N-acetyl-p-benzoquinone, by filling the depleted glutathione stores. . The mortality of amanita mushroom poisoning varies between 10-30%. Wilson Disease is 100% mortal if liver transplantation is not performed.

Acute liver failure is characterised by sudden onset hyperbilirubinemia, hepatic encephalopathy (HE), coagulopathy in individuals without any known liver disease. It is a clinical syndrome characterized by high morbidity and mortality [1]. In patients with a diagnosis of chronic liver disease, an acute liver failure can be encountered on chronic ground. In the United States (USA), ACF affects approximately 2000-2800 individuals each year and accounts for 5-6% of liver transplantation causes [2]. duration is important.

Keywords: *Hepatic; Acute; Failure*

O'grady and Ark. [3] Aky According to the Classification of the Environmental Development Period of Humanity and Ensefalopathy

a. Hyperacute: 0-7 days
b. Acute: 8-28 days
c. Subacute: 29-84 days

The higher the onset rate of the disease in AHF; that is, the shorter the time of development of encephalopathy, the greater the chances of spontaneous healing of patients. The survival of patients varies between 10-90% without liver transplantation. The last benefit is proven treatment modality. In the studies performed, it was observed that the one-year survival of the patients increased from 50% to 75%. Most drugs and herbal products are caused by hepatotoxicity.

Etiology

a. Virüs
b. Medicines and toxins
c. Other reasons

Reasons for Viral

a. HBV (It constitutes a large part of the viral factors causing AHF.)
b. HAV (The risk is at least this, but the risk increases as the age of exposure to the virus increases.)
c. HDV (Risk increases in cases of superinfection or co-infection.)
d. HCV (Rarely causes.)
e. HEV (It is more common in Asian and European countries. May cause 20% AKY in 3rd trimester pregnant women.
f. HSV-1
g. HSV-2
h. VZV
i. EBV
j. 10.CMV
k. HPV-6
l. Parvovirus B19

Drugs and Toxines: The most drugs and herbal products cause hepatotoxicity

Acetaminophen is the most common agent causing liver damage. It can cause fatal liver necrosis with direct hepatotoxic effect at doses above 7-10g/day.

Acetaminophen toxicity impairs the liver detoxification mechanism. When the drug is taken in an overdose, the glutathione stores are insufficient and the toxic metabolite of the drug 'N-acetyl-p-benzoquinone' (NAPQI) binds to cytoplasmic proteins, causing hepatocellular necrosis.

a. Phenytoin
b. amoxicillin-clavulanate
c. Erythromycin
d. Sulfonamides
e. Halothane
f. Dapsone
g. Diclofenac,
h. 8 Carbamazepine
i. Sulindac
j. isoniazid
k. ketoconazole
l. Disulfiram,
m. Valproic acid
n. Amiodarone
o. The mortality of Amanita mushroom poisoning varies between 10-30%. Amanitin toxin enters enterohepatic recirculation, disrupts hepatocyte mRNA synthesis and causes hepatotoxicity in a dose-dependent manner."
p. Basillus cereus
q. Carbon tetra chloride [4]

Acute Oil Liver Disease and Help Syndrome of Pregnancy

It is usually seen in the 3rd trimester. In the fetus, "3-hydroxyacyl-coenzym-A dehydrogenase" is thought to be due to the accumulation of medium and long chain fatty acids in the mother as a result of enzyme deficiency. Preeclampsia (HT and proteinuria) can be seen. Maternal mortality is 50%, Fetal mortality is between 42-49%. Urgent OCT may be required in postpartum period in patients without response [5].

Other Reasons

Acute autoimmune hepatitis

Wilson Disease: If liver transplantation is not performed, it is 100% mortal. The Kayser-Fleischer ring may not be seen in 50% of patients. There are increased urinary copper and variable serum copper levels. Serum ceruloplasmin levels are normal in 15% of patients. Often coombs-negative hemolytic anemia, severe hyperbilirubinemia, moderate transferase height, high serum and urine copper concentrations may accompany.

Ischemic liver disease ("shock liver")

a) Budd-Chiari
b) Venooclusive diseases
c) Malignant infiltration
d) Sepsis
e) Heat stroke
f) cryptogenic

Diagnosis Specific cause should be determined quickly:

a. Mental status assessment should be done
b. PT / INR measurement should be done
c. Mental status change and prolonged PT (> 4-6 s), INR (> 1.5) values require hospitalization.
d. Blood ammonia level is prognostic.
e. lactate level (poor prognosis if Ph <7.3)
f. Percutaneous liver biopsy is generally not recommended due to bleeding disorders.
g. Biopsy is a rarely used method since the histological findings will not change the course of the treatment.

Clinical

Clinical findings in early period are nonspecific. The degree of serum aminotransferase height and recovery rate are not indicative for prognosis. The correction of aminotransferases and the deterioration of bilirubin and PT / INR values are an important signal for liver failure. Sudden severe hepatocyte loss, multiorgan failure and death due to complications can be seen.

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Clinical

Clinical findings in early period are nonspecific. Hepatıc Ensefalopathy And Braın Edema for prognosis of the degree of serum aminotransferase elevation and recovery rate. Ammonia, mercaptans, GABA, endogenous benzodiazepines, serotonin / tryptophan are thought to be due to pseudo-neurotransmitters, varying receptor activations (NMDA) and GABAergic repetition. [6]. Toxins due to disruption of the blood-brain barrier easily pass into the cerebrospinal fluid. Detoxification of ammonia is carried out in astrocytes in the brain, ammonia is converted into glutamine. Causes lactate accumulation + dentricarboxylic acid cycle activity decreases, + production of phosphate compounds: energy production decreases Suddenly, astrocytes swell, resulting in brain edema. Free oxygen radicals cause cellular dysfunction in astrocyte mitochondria. Cerebral autoregulation disappears due to changes in peripheral blood pressure, and cerebral perfusion is disturbed. Inflammatory cytokines pass through the impaired blood-brain barrier, further aggravating the condition. It was observed that the level of arterial ammonia> 200 mcg / dl was associated with cerebral herniation and death. The results are worse as the stage increases, and brain edema is observed in approximately 80% of patients with stage 4 hepatic encephalopathy. Increased intracranial pressure causes

decreased cerebral perfusion pressure and ischemic brain damage or brainstem herniation, which explains half the mortality in ESR [7].

The head of the bed should be raised 30 degrees and the patient should be taken to a quiet, quiet room

In patients who need mechanical ventilator support, hyperventilation (PaCO2; 25-30 mmHg) should be applied to reduce intracranial pressure. Hyperventilation reduces cerebral edema episodes but does not delay herniation development. Likewise, lactulose has not been shown to improve the survival of AKY, but has been shown to help extend survival in stage 1-2 HE [8]. Irreversible brain damage develops if values hover over these limits for 2 hours. Mannitol is an established osmotic agent that positively affects survival, but its use in kidney failure is limited. Thiopental, phenytoin, phenobarbital can be applied [9].

Coagulopathy and Trombocytopenıa

a. F synthesized from the liver develops following the deficiency of 2, 5, 7,9).
b. Protein C, S may also occur due to underproduction of anti-thrombin III factors.
c. Hypofibrinogenemia (hemorrhages may occur at values below 100mg/dl)
d. PT / INR is the easiest and most sensitive test showing prognosis during illness
e. The platelet count is below 100,000 in about 70% of patients, but rarely drops below 25,000 [10].

Pulmonary Complıcatıons

a. Bleeding
b. Pleural effusion,
c. Atelectasis,
d. Intrapulmonary shunts
e. Acute lung injury occurs in 40% of patients and causes significant morbidity and mortality.
f. Sepsis
g. Bleeding
h. Pleural effusion
i. Atelectasis
j. Intrapulmonary shunts can cause breathing difficulties.
k. Acute lung injury occurs in 40% of patients and causes significant morbidity and mortality.

Renal Disorders Kidney failure can be seen in 70% of patients and the reason is multifactorial. Renal dysfunctions due to causes such as dehydration, acetaminophen and direct toxicity of NSAIDs, hypotension, sepsis, DIC. SIRS triggers renal dysfunction in ACY that is not related to acetaminophen. If necessary, early period dialysis is performed [11].

Hemodynamic Dısorders

Hyperdynamic circulation is common in AKY. Systemic and pulmonary vascular resistance decreases, cardiac output increases, and eventually hypotension occurs.It may be seen due to endotoxins, tumor necrosis factor, and often low oral intake and dehydration. Acidosis develops as a result of impaired oxygen transport and use to the periphery.

Infection and Sepsis

a. Due to opsonization defect, complement deficiency and immunosuppression, the natural immune system is disturbed in ACF.
b. The risk of infection is the highest in subacute AKY, and this risk increases with the duration of stay in the intensive care unit.
c. Infection causes death in 37% of patients.
d. Infections worsen hepatic encephalopathy and brain edema.

Electrolyte and Acid-Base Disorders

a. Hyponatremia (As a result of the decrease in free water clearance and renal sodium reabsorption)
b. Hypopotassemia
c. Hypophosphatemia (Loss from kidney is seen. Continuous serum phosphate elevation may be related to poor prognosis in ACY induced by acetaminophen toxicity.)
d. Acid-base disorders can be commonly encountered.

Hypoglycemia

a. It can be seen in 45% of patients with FFM.
b. Decreased destruction of insulin in the liver occurs due to the mobilization of glycogen stores and disorders in gluconeogenesis.
c. Normoglycaemia should be ensured

Gastroıntestınal Bleeding

The risk of gastrointestinal bleeding is increased in AKY. Morbidity and mortality have been shown to decrease with prophylactic treatment, so they should be considered in standard therapy [12].

Treatment

N-Acetyl System

If it is used as an antidote in acetaminophen toxicity in the early period, it effectively prevents the hepatotoxicity and ACY made by the toxic metabolite of acetaminophen, N-acetyl-p-benzoquinone, by filling the glutathione stores. Serious hepatotoxicity can be prevented if administered within 8-10 hours following acetaminophen toxicity. Thus, the mortality rate can be reduced to less than 1% by applying NAS treatment to these patients in the early period. Although the benefit of NAS treatment is not yet fully known in ACY, which is not related to acetaminophen, it appears to be beneficial in children. In a multi-center, randomized controlled study; it has been shown to improve survival in a group of adults with stage 1-2 HE [13,14]

Penicille And Silicın

During the disease, it is effective to use penicillin G 250mg/kg/day and silibinin 20-50mg/kg/day early, but in severe cases, emergency orthotopic liver transplantation (OCT) may be required.

Nucleosid Analogs

The efficacy of antiviral drugs has not yet been confirmed in ESR due to hepatitis B virus infection, but in a randomized controlled study, significant clinical benefits were achieved in 71 acute HBV patients, 3 of whom were using lamivudine, and HE was.It was reported that the use of entecavir was well tolerated

and positively affected the course of the disease in 6 patients with HBV-related ACF [15].

Acyclovir

If HSV is suspected, IV acyclovir is both well tolerated and a useful treatment method.

Plasmaferease and D-Penıcılamıne

The use of D-penicillamine, trientin and zinc is not very beneficial in Wilson disease, which has advanced to AKY. Patients until OCT.They may benefit from plasmapheresis, but this treatment method has also been shown to have no positive effect on surveillance [16,17].

Liver Support Systems

A. Non-biological: It is based on the principle of filtering toxins through hemodialysis.

1. Continuous renal replacement treatments (continuous veno-venous hemodialysis, continuous veno-venous hemofiltration, continuous veno-venous hemodiafiltration, continuous slow ultrafiltration, continuous high-change dialysis, continuous plasma filtration adsorption)
2. Plasmapheresis and plasma changes
3. Hemoperfusion
4. Liver replacement therapy (Mars and Prometheus): Dials toxins bound to MARS (Molecular Absorbent and Recirculating System). This system effectively removes water-soluble compounds (ammonia, lactate, creatinine, urea) and fat-soluble compounds (bile acids, aromatic amino acids, bilirubin, short and medium chain fatty acids).

It has been observed that both systemic and cerebral hemodynamic parameters are improved in patients with HF and HF developed on AKY and chronic ground [18,19].

It has been observed that non-biological systems improve HE in AKY, but they do not have any benefit on mortality, and it has been found that they affect positively the results in developed AKY on chronic basis [20].

B. Biological: By using various cell (hepatocyte) cultures, a detoxification environment is tried to be created close to natural liver tissue.

C. Biyo-artificial (hybrid):

Liver Transplantatıon

Liver transplantation is the most important and modern treatment method with proven effectiveness in AKY. Uncontrolled sepsis, severe respiratory failure, excessive inotropic agent requirement, metastatic cancer, active alcoholism, drug addiction and psychosocial causes are contraindicated conditions for transplantation. In patients with liver transplantation, the survey was 90% in stage 1 HE, 77% in stage 2, 79% in stage 3, and 54% in stage 4. [21,22].

Prognosıs

The factor that causes AHF is the most important factor that determines the prognosis. The lowest mortality rate is observed in acetaminophen toxicity (30%) and in the AHF (50%) due to HAV. The degree of HE gives an idea about mortality. Stage 2 HE has 30% mortality rates, stage 3 HE 45-50% and stage 4 80% mortality rates. Patients who developed rapid HE had a better chance of recovery than patients who developed encephalopathy in a longer period of time, and their surveys were found to be longer without the need for OCT. Many prognostic systems have been developed to determine spontaneous survival. The most widely used of these is King's College criteria.

Kıng's College Crıterıa

1. Acetaminophen-associated AHF

   Arterial Ph <7.3 (independent of HE)

   PT> 100 sec, INR> 6.5

   Serum creatinine> 3.4mg/dl

   Grade 3-4 HE
2. Acetaminophen-free AHF

   PT> 100 sec, INR> 6.5 (independent of HE) (for OCT list)

   Age <10 or> 40

   Serum bilirubin> 17.4mg/dl

   Etiology (non-A, non-B hepatitis, drug reax.)

   PT> 50 sec, INR> 3.5

   Between jaundice and HE> 7 days

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