MANUAL:		POLICY #:			
SUBJECT:	**Guidelines for the diagnosis and management of ICU patients with acute liver failure (ALF)**	EFFECTIVE DATE:			
		REVISED DATE:			
		AUTHORIZED APPROVAL:			
PERSONNEL COVERED:	**Nursing and physician care providers of relevant patients in intensive care unit environments**	PAGE:	1	OF	5

PURPOSE

The purpose of this policy is to provide clinical guidelines for the diagnosis and management of ICU patients with ALF. ALF is a rare condition with varied etiologies that often affects young persons and carries a high morbidity and mortality. The appropriate use of liver transplantation and medical management of patients with ALF has dramatically improved survival. No single therapy has been found to improve the outcome of all patients with ALF with the possible exception of N-acetylcysteine (NAC).

DEFINITION

- *ALF is defined as*:
  - International Normalized Ratio (INR) $\geq$ 1.5 *and*
  - Any degree of mental alteration (encephalopathy) in a patient without pre-existing cirrhosis (exception Wilson's disease or HBV) in a disease < 26 weeks duration

- *King's College Criteria* may be used to determine the appropriateness of listing a patient for orthotopic liver transplantation (OLT). These criteria include:
  - *Acetaminophen-induced ALF:*
    - Strongly consider OLT listing for arterial lactate >3.5 mmol/L after early fluid resuscitation
    - List for OLT if: pH <7.3 or arterial lactate > 3.0 mmol/L after adequate fluid resuscitation
    - List for OLT if all three occur within a 24-hour period:
      - Grade III or IV encephalopathy
      - INR > 6.5 *and*
      - Creatinine > 3.4 mg/dL
  - *Non-acetaminophen-induced ALF:*
    - List for OLT if:
      - INR > 6.5 and encephalopathy present (any grade) *OR*
      - Encephalopathy present (any grade) *and* three of the following:
        - Age <10 or > 40 years
        - Jaundice for > 7 days before development of encephalopathy
        - INR $\geq$ 3.5
        - Serum bilirubin $\geq$ 17 mg/dL
        - Unfavorable etiology, such as:
          - Wilson Disease
          - Idiosyncratic drug reaction
          - Seronegative hepatitis

- *Grades of Encephalopathy:*
  - *Grade I*: Changes in behavior with minimal change in level of consciousness
  - *Grade II*: Gross disorientation, drowsiness, possibly asterixis, inappropriate behavior
  - *Grade III*: Marked confusion: incoherent speech, sleeping most of the time but arousable to vocal stimuli
  - *Grade IV*: Comatose, unresponsive to pain, decorticate or decerebrate posturing.

POLICY

- This policy governs the following:
  - General principles of ALF diagnosis and treatment
  - Disease-specific principles of ALF diagnosis and treatment:
    - These include malignancy, viral, drug (including acetaminophen), toxin, pregnancy-related, autoimmune, ischemic, and thrombotic etiologies of ALF as well as Wilson's disease.
  - Organ system-specific principles of ALF diagnosis and treatment:
    - These pertain to the central nervous system, cardiovascular, renal, hematologic, infectious diseases and metabolic systems.
  - Patients with ALF will be admitted to an ICU setting unless they or their surrogates have indicated that they do not wish to undergo aggressive diagnostic and therapeutic interventions.
  - The precise etiology of ALF will be sought if it possible to determine. To facilitate this, the following laboratory studies may be obtained: chemistry 7 with calcium, magnesium and phosphorus, liver function tests including bilirubin, coagulation studies, viral hepatitis serologies, autoimmune hepatitis markers such as ANA, arterial blood gas, arterial lactate, complete blood count, ammonia level, amylase, lipase, ceruloplasmin level, serum and urinary copper levels, toxicology screen, acetaminophen level and blood type and screen. It may be necessary to perform a liver biopsy to establish an etiology of ALF.
  - The liver transplant service will be contacted in timely fashion to determine whether transplantation is or could be indicated.

EQUIPMENT

- ICU patients will undergo hemodynamic and neurologic monitoring as described below utilizing routine ICU devices.

PROCEDURE

- *Disease-specific principles of ALF diagnosis and treatment*:
  - Malignancy history may warrant special imaging and a liver biopsy
  - Viral:
    - Patients with ALF due to herpes or varicella zoster virus will should receive acyclovir (5-10 mg/kg IV every 8 hours)
    - Patients with ALF due to HBV will receive nucleoside analogues:
      - Entecavir (preferred in renal insufficiency): 0.5 mg po daily *OR*
      - Tenofovir: 300 mg po daily *OR*
      - Lamividine: 100 mg po daily *AND*
      - Adefovir: 10 mg po daily
  - Drug:
    - Patients with a known or suspected acetaminophen overdose within four hours of presentation will be give activated charcoal prior to NAC
    - Patients will be given NAC and details regarding the amount and timing of all prescription and non-prescription drugs will be obtained:
      - *For oral regimen*:
        - Load with 140 mg/kg then administer 70 mg/kg q 4 hours for 17 doses
      - *For intravenous regimen*:
        - Load with 150 mg/kg in 200cc D5W over 15 minutes then administer 50 mg/kg in 500 cc D5W over 4 hours then administer 100 mg/kg in 1000 cc D5W over 16 hours
  - Toxin
    - NAC will be administered in ALF patients with known or suspected mushroom poisoning

- Pregnancy-related
  - Emergent obstetric consultation will be obtained
- Autoimmune (hepatitis)
  - Prednisone (40-60 mg/day) will be administered
- Ischemic
  - Advanced cardiac monitoring will be considered
- Thrombotic
  - An ultrasound of the hepatic and portal veins will be obtained
- Wilson's disease
  - Ophthalmology will be consulted for a slit lamp examination as appropriate

- *Organ system-specific principles of ALF diagnosis and treatment*:
  - Central nervous system:
    - Hourly neurological examination will be conducted. A brain CT may be considered to exclude other causes of decreased mental status.
    - Seizures will be treated with phenytoin and short-acting benzodiazepines. Seizure prophylaxis will not be performed.
    - Sedation will be avoided or minimized.
    - In those with low grade encephalopathy (Grades I and II):
      - Oral or rectal lactulose will be administered cautiously to effect a bowel purge but not cause diarrhea or abdominal distension.
    - In those with high grade encephalopathy (Grades III and IV):
      - Elective endotracheal intubation will be performed.
      - Neurosurgical consultation will be obtained to request intracranial pressure (ICP) monitoring.
      - In those at highest risk for cerebral edema (serum ammonia > 150 mcg/dL, acute renal failure, need for pressors), prophylactic hypernatremia to a sodium level of 145-155 mEq/L will be induced. The head of the bed will be elevated.
      - In those with ICP > 20:
        - Intravenous mannitol (0.5-1.0 gm/kg) will be administered as first line therapy
        - Further treatment may require induction of a barbiturate coma or
        - Institution of therapeutic hypothermia to a core body temperature of 34-35 degrees C.
  - Cardiovascular system:
    - Pulmonary artery catheterization is rarely indicated. Hemodynamic data may be obtained from noninvasive and minimally invasive devices as delineated in the monitoring guidelines
    - Resuscitation will be delivered to achieve a MAP of $\geq$ 75 mm Hg and/or a CPP of 60-80 mm Hg:
      - Hypotension is first treated by fluid resuscitation where adequate intravascular volume should be achieved and maintained. This is best accomplished by administration of intravenous normal saline
      - Norepinephrine will be administered for volume-refractory hypotension or to ensure adequate CPP. Vasopressin will be added in norepinephrine-refractory cases.
  - Renal system:
    - If dialysis is needed for acute renal failure, a continuous mode will be employed
    - Nephrotoxic agents will be avoided

- Hematologic system:
  - Platelets and coagulation factors will be restored via transfusion of platelets and FFP in the face of active bleeding or the need to perform invasive procedures as delineated in the transfusion guidelines. In addition, the use of Factor VII and/or Prothrombin concentrate complex (PCC) may be considered
  - Vitamin K will be given (5-10 mg subcutaneously)
  - Stress ulcer prophylaxis will be administered with either H2 receptor antagonists or proton pump inhibitors
- Infectious diseases
  - Surveillance cultures will be obtained early to detect bacterial and fungal pathogens as early as possible. Antibiotics will be initiated promptly according to surveillance culture results at the earliest sign of active infection or deterioration as manifested by progression to high grade encephalopathy or development of the systemic inflammatory response syndrome (SIRS) as described in the Sepsis Guidelines. There is no role for prophylactic antibiotics or antifungals in the absence of high grade encephalopathy or SIRS.
- Metabolic system:
  - Glucose, phosphate, potassium and magnesium levels will be monitored and corrected frequently
  - Adequate nutritional status will be monitored and maintained. Enteral nutrition will be given, if possible.
  - There is no role for routine use of commercial liver support systems

PERFORMANCE REVIEW

The ICU director along with the multidisciplinary team will meet on a regular basis to identify and address issues through quality assurance and continuous quality improvement activities. The SICU database will track relevant patient data. This information will be reviewed and discussed regularly to identify opportunities for improvement.

DISCLAIMER

These clinical guidelines may not be appropriate for all patients under all circumstances. New information and evidence may become available that renders their content less valid. Practitioners must utilize their clinical judgment to determine what is helpful to them and what is appropriate.

REFERENCE(S)

- Acute Liver Failure Guidelines, 2012. American Association for the Study of Liver Diseases (AASLD). International Guidelines Center, Baltimore, MD.

RELATED POLICIES AND PROCEDURE(S)

- ALF order set
- Monitoring guidelines
- Transfusion guidelines
- Sepsis guidelines

Effective/Revision Dates for Policy # <insert policy number>		
Effective:	00/00/0000	<replace with revising committee name>
Revised:	00/00/0000	
	00/00/0000	
	00/00/0000	
Keywords:		