Table 4. Specific pharmacological therapies for management of alcoholic hepatitis

A) Therapies with proven efficacy
1. Corticosteroids
2. Nutritional supplementation
B) Therapies with potential efficacy
1. Pentoxifylline
2. *N*-acetyl cysteine
3. Granulocyte colony stimulating factor
C) Therapies with no efficacy
1. Tumor necrosis factor-α inhibitors
2. Antioxidant cocktail and vitamin E
3. Hepatic mitogens: insulin and glucagon, anabolic steroids
4. Propylthiouracil

score (76). The North American Consortium for Study of End Stage Liver Disease-Acute on Chronic Liver Failure (NACSELD ACLF) score is the easiest to use—patients with two or more extra-hepatic organ failures, second infections, and higher MELD score are at greatest risk of mortality (77).

Sepsis surveillance should be performed and broad-spectrum antibiotics should be administered before transfer to the ICU, or within one hour of admission. The choice of antibiotics depends on prevailing local antimicrobial resistance patterns. Piperacillin-tazobactam is generally the preferred drug used for sepsis, although vancomycin and meropenem may be considered in patients with penicillin hypersensitivity. As sepsis is difficult to diagnose in this group and about 40– 50% of patients may be culture negative, there should be a low threshold for diagnosis of infection and initiation of antibiotic therapy. Diagnosis of infections in patients with AH and cirrhosis should be performed using standardized definitions and guidelines (78). It is important to differentiate community acquired infections from nosocomial infections (onset after 48 h of admission to hospital) or healthcare-associated infections (within first 48 h of admission in patients with hospitalization within past 6 months, clinic visit within past 30 days, or those residing in nursing homes), as the empiric antibiotics for nosocomial or healthcare-associated infections should cover broadly for multidrug resistant bacteria, and in select high-risk cases for atypical organisms and fungal infections.

Ulcer prophylaxis is recommended using proton pump inhibitors. Both proton pump inhibitors and H2 antagonists increase the risk of infections such as aspiration pneumonia and clostridium difficile, but decrease the risk of chemical pneumonitis and gastrointestinal bleeding. Proton pump inhibitors are superior to H2 antagonists for the prevention of gastrointestinal bleeding. Glucose control is targeted to levels <200 mg/dL and transfusion is required with the hemoglobin target of 7–8 g/dL.

Organ failure scores are used to determine severity of acute on chronic liver failure. Patients with renal failure and acute kidney injury should receive diligent care with the aim to identify and reverse precipitating factors and improve renal function. Renal replacement therapy is recommended in the presence of acute kidney injury in the presence of sepsis-associated acute tubular necrosis, or if the cause of acute kidney injury is unclear. In the presence of hepatorenal syndrome, a therapeutic trial of renal replacement therapy may be considered in patients who are potential liver transplant candidates. Patients requiring pulmonary support should receive low tidal volume to avoid lung injury. Vasoconstrictors and pressor may be needed to maintain mean blood pressure of >65 mm Hg.

Specific pharmacologic therapies. Pharmacological therapies examined for AH patients are listed in **Table 4**.

Recommendations

7. Patients with severe AH should be treated with corticosteroids if there are no contraindications for their use (Strong recommendation, moderate level of evidence)
8. The existing evidence does not support the use of pentoxifylline for patients with severe AH. (Conditional recommendation, low level of evidence)

Key concepts and statements

14. Response to treatment with corticosteroids should be determined at 7 days using the Lille score. Treatment should be discontinued among non-responders to therapy, defined as those with a Lille score >0.45
15. Patients non-responsive to corticosteroids, ineligible for early LT, and with multiple organ failures may be considered for palliative therapy.

Corticosteroids. As the first randomized controlled study to assess efficacy of corticosteroids in the treatment of AH in 1971 (79), a total of 14 randomized studies (12 against placebo, 1 against enteral supplementation, and 1 against antioxidant cocktail) have reported conflicting data, likely to be due to variations on inclusion/exclusion criteria and the use of liver biopsy for confirming the diagnosis of AH (61,79–90). In a pooled analysis, using individual patient data from the five largest randomized controlled studies (85–88,91), corticosteroids provided survival benefit at 28 days (80% vs. 66%, $P<0.0001$) in half of the patients (92). The largest randomized placebo controlled multicenter study from the United Kingdom (the STeroids Or Pentoxifylline for Alcoholic Hepatitis (STOPAH) study) on 1,103 severe AH patients showed only a trend for mortality benefit at 28 days with prednisolone, compared with patients receiving placebo (13.8% vs. 18%, $P=0.056$). A meta-analysis of randomized studies (including the STOPAH study) showed that corticosteroids were effective in reducing short-term mortality by 46%.

Prednisolone is preferred over prednisone, as the latter requires conversion to prednisolone, which may be impaired in patients with impaired liver synthetic function. Moreover, prednisone did not improve patient survival in a randomized clinical trial (89). Prednisolone is used in a dose of 40 mg per day for a total duration of 4 weeks. Methylprednisolone 32 mg per day by intravenous route is used for patient unable to take oral medications. There are no studies examining different doses