Alcoholic hepatitis: Pathogenesis and Therapeutic Targets

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Alcoholic hepatitis (AH) is a severe form of alcoholic liver disease with high mortality. The pathogenesis of AH is not fully understood, but it is generally believed that inflammation is a key factor leading to liver failure in AH. Steroids, which have broad immunosuppressive effects, have been used for the treatment of AH over the last forty years. Steroids elicit modest improvement in short-term survival rate in patients with severe AH but also cause severe side effects. Several specific inflammatory targets (e.g., IL-1, LPS, and gut microbiota) are currently under investigation for the treatment of AH in combination with reduced doses of steroids. In addition to inflammation, impaired liver regeneration is another major cause of liver failure in AH, which deteriorates further after steroid treatment because inflammation plays a key role in promoting liver repair. Interleukin-22 (IL-22) is a promising drug for the treatment of AH because of its hepatoprotective and anti-fibrotic functions and relatively few side effects. In addition, IL-22 treatment also ameliorates bacterial infection and kidney injury, two major complications associated with severe AH. Combination therapy of steroids plus IL-22 is currently under investigation in preclinical and clinical studies and may hold great promise for AH by providing more beneficial effects and fewer side effects than single drug treatment.