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**Corticosteroid and nucleoside analogue for hepatitis B virus-related acute liver failure**

Fujiwara K *et al.* Combination therapy for HBV-ALF

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**Abstract**

The early introduction of combination therapy of high-dose corticosteroid and nucleoside analogue is beneficial for the rescue of severe acute exacerbation of chronic hepatitis B.

**Key words:** Chronic hepatitis B; Exacerbation; Acute liver failure; Nucleoside analogue; Corticosteroid

**Core tip:** Nucleoside analogues generally need some weeks before hepatitis B virus DNA becomes undetectable and therefore they may be too slow to influence the clinical course of acute severe liver failure, and the overwhelming anti-viral immune response might actively contribute to the effectiveness of treatment. We have performed prospective study of early introduction of high-dose corticosteroid with/without nucleoside analogue for severe acute reactivation of chronic hepatitis B since 1997, and recovery rate without liver transplantation improved from 25% to 70%.

## TO THE EDITOR

We read with interest a case report by Bockmann *et al*<sup>[1]</sup>, who presented three patients with hepatitis B virus (HBV)-related acute liver failure (ALF) who were treated with combination of high-dose corticosteroid (CS) and nucleoside analogue (NA), which resulted in a rapid improvement of clinical and liver parameters.

We agree with authors' insight that NAs generally need some weeks before HBV-DNA becomes undetectable and therefore they may be too slow to influence the clinical course of acute severe liver failure, and that dampening the overwhelming anti-viral immune response might actively contribute to the effectiveness of treatment.

There is no proven beneficial treatment, except for emergency liver transplantation (LT) for ALF because of severe acute reactivation of chronic hepatitis B (SAECHB). In Japan where shortage of donor livers have been serious problem, we have performed prospective study of early introduction of high-dose CS with/without NA for SAECHB since 1997, and recovery rate without LT improved from 25% to 70%<sup>[2-5]</sup>, but have rarely seen publications from European countries and US after controlled trials of CS in the 1970s had shown no improvement in survival, although the first impressive case report of successful CS therapy for SAECHB was published in Europe<sup>[6]</sup>.

When discussing HBV-related ALF, we should distinguish that due to acquired infection and that due to reactivation of chronic infection because of the differences of the level and continuity of viral replication and as a consequence the efficacy of therapy<sup>[7]</sup>. The latter patients are much more resistant to therapy than the former ones.

In our study, most of the patients did not recover when the start of combination therapy was delayed beyond 10 d after the diagnosis of severe disease, because large numbers of hepatocytes would already have been destroyed and inhibition of inflammatory reaction might not be effective. On

the other hand, we have often experienced patients with SAECHB showing very high level of viral replication more than 8-9 logcopies/ml of HBV. In such cases, control of both HBV and liver tests was quite difficult even using the combination therapy, and many cases developed fulminant liver failure and impaired liver regeneration resulting in death due to liver failure or infectious complications, or LT.

The number of patients with SAECHB has decreased by early use of NA before the development of severe disease, but HBV replication has been shown to persist in the liver and in peripheral blood mononuclear cells even in patients with resolved HBV infection (HBsAg negative, HBsAb and/or HBcAb positive), and reactivation of HBV could occur in relation to immunosuppressive therapy and chemotherapy. In the future, we should re-evaluate the efficacy of combination therapy by worldwide/multicenter studies using "uniform criteria and treatment protocols", although controlled trials will not be feasible considering the poor prognosis.

## ACKNOWLEDGEMENTS

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## Footnotes

**Conflict-of-interest statement:** Osamu Yokosuka has received research funding from Chugai Pharma.

## Figure Legends