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Glucocorticosteroids in acute alcoholic hepatitis: The evidence of a beneficial effect is getting even weaker

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The effect of glucocorticosteroid therapy in acute alcoholic hepatitis has been debated for more than 40 years [1–4]. Although a large number of controlled clinical trials have been performed, there is still insufficient evidence to support glucocorticosteroids for patients with alcoholic hepatitis [4]. Since autoimmunity is not a significant feature of this disease, the rationale behind the use of glucocorticosteroids, is to block cytotoxic and inflammatory pathways [5]. However, the potential side-effects of glucocorticosteroids are numerous including anti-anabolism, muscle breakdown (proteolysis), immunosuppression, increased susceptibility to infection, and increased risk of GI bleeding.

Originally, glucocorticosteroids were claimed to benefit any patient with alcoholic hepatitis. Later the beneficial effect was restricted to those with hepatic encephalopathy, later again, to those with a Maddrey discriminant function $\geqslant 32$. Most recently, the group with a claimed beneficial effect of glucocorticosteroids has been reduced even further. In a study from Glasgow the beneficial effect was confined to the subgroup of patients with a Maddrey discriminant function $\geqslant 32$ *and* a Glasgow alcoholic hepatitis score $\geqslant 9$ [6]. However, this study was not performed as a controlled study. In the minority of the patients, who were included in randomised controlled trials, there was no significant beneficial effect of glucocorticosteroid therapy in the subgroup in question [6].

Recently the so-called Lille prognostic model has been used to identify 'responders' and 'non-responders' to glucocorticosteroid therapy in alcoholic hepatitis [7]. This model has been developed and validated *exclusively* for glucocorticosteroid treated patients [7]. The predominant variable in the Lille model is the one week change in bilirubin. A decrease in this variable from day 0 to day 7 is considered a major indicator of being a 'responder' to glucocorticosteroid therapy. The 'non-responders', according to the Lille model, have a six month survival of only 25% on glucocorticosteroid therapy [7].

In a recent meta-analysis based on individual data from the five latest randomised controlled trials, the beneficial effect of glucocorticosteroids was confined to the subgroup of 'responders' according to the Lille model [8]. The 'non-responders' according to the model had no significant effect from glucocorticosteroid therapy. The problem with this analysis is that the Lille model has only been shown to apply to glucocorticosteroid treated patients. The control groups in this meta-analysis were not treated with glucocorticosteroids and the Lille model may not apply to those patients. Most likely the coefficients in the model would be different in the control patients. There could even be an interaction between the therapy (glucocorticosteroid/control) and the variables included in the model calling for a comprehensive analysis based on data from both treatment and control patients [9]. Considering all these reasons, the results of this meta-analysis seem questionable. Furthermore, the study was based on a selected part of the available trials [4], possibly suggesting a selection bias.

The Lille group has recognized that infections may be a serious problem of glucocorticosteroid therapy in alcoholic hepatitis [10]. Nevertheless, it has been suggested that all patients with the disease should have at least one week of glucocorticosteroids to see if they would be 'responders' (decrease in bilirubin from day 0 to day 7) according to the Lille model. This strategy implies that potential 'non-responders' would need to receive one week of therapy, which may be deleterious, and possibly lead to a six month survival probability of only 25% [7]. Such a strategy seems very problematic.

Over the years the evidence in favour of glucocorticosteroid therapy in alcoholic hepatitis has steadily decreased, and now it seems to be the time to move on to other therapies with more potential, e.g., pentoxifylline.

Conflicts of interest

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