Hepatitis aguda alcohólica: Yo uso corticoides

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I have no conflict of interests related to this presentation
Corticosteroids in patients with severe alcohol related hepatitis

• Several studies in the last 30+ years
• Conflicting results, risk of infection...
• Should we use it? Let’s see what the guidelines say...
Patients with severe disease (DF>32, with/without HE) and lacking contraindications to steroid use should be considered for prednisolone (40 mg/day for 28 days) (Class I, level A).

ACG Clinical Guideline: Alcoholic Liver Disease

YES, YOU SHOULD

Recommendations

Patients with severe AH should be treated with corticosteroids if there are no contraindications for their use (Strong recommendation, moderate level of evidence)

Singal AK, et al. Am J Gastroenterol 2018
In the absence of active infection, corticosteroids (prednisolone 40 mg/day or methylprednisolone 32 mg/day) should be considered in patients with severe AH to reduce short term mortality (Grade A1).
But...what if all the guidelines got it wrong?

It would be nice if we had an up-to-date meta-analysis of individual patient data to end this controversy
Corticosteroids Reduce Risk of Death Within 28 Days for Patients With Severe Alcoholic Hepatitis, Compared With Pentoxifylline or Placebo—a Meta-analysis of Individual Data

Alexandre Louvet, Mark R. Thursz, Dong Joon Kim, Julien Labreuche, Stephen Atkinson, Sandeep Singh Sidhu, John G. O’Grady, Evangelos Akriviadis, Emmanouil Sinakos, Robert L. Carithers, Jr., Marie-José Ramond, Willis C. Maddrey, Timothy R. Morgan, Alain Duhamel, Philippe Mathurin

To appear in: Gastroenterology
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Metanalysis of Individual Patient Data

Primary outcome: overall survival at 28 days

Studies were selected if:

• Randomized
• Published as full articles
• Written in english
• Patient data on Maddrey DF >32 or encephalopathy

Louvet A, et al. Gastroenterology 2018
Metanalysis of Individual Patient Data

Corticosteroids vs Controls:

6 RCT (956 patients)

N=490 corticosteroids

N=466 controls

Corticosteroid use was significantly associated with a decrease in mortality rate at 28 days by comparison to controls (also vs pentoxifylline)

Louvet A, et al. Gastroenterology 2018
Corticosteroids vs Controls (6 trials; N=956 patients)

Louvet A, et al. Gastroenterology 2018
Metanalysis of Individual Patient Data

A significant survival benefit was observed during the 28-day therapeutic period.

Result provides a strong argument supporting the use of prednisolone for severe alcohol related hepatitis.

Author’s statement:

We feel that the present metanalysis ends the controversy surrounding corticosteroid treatment.

We hope that the hesitation about their use in severe alcoholic hepatitis will decrease over time.

Louvet A, et al. Gastroenterology 2018
OK, I am convinced:
Corticosteroids increase survival in the first 28 days of severe AH

However, improving survival only in the first month is enough to compensate for the risks involved? What about long-term?
Main Drivers of Outcome Differ Between Short Term and Long Term in Severe Alcoholic Hepatitis: A Prospective Study

28d corticosteroids

Severity at baseline
Response to treatment at day 7

Severe AH → Alive at 6 months

Alcohol relapse

No alcohol relapse
Initial non response to treatment

No alcohol relapse
Initial response to treatment

Minimal risk of death

Substantial risk of death

High risk of death with an additional effect in case of initial non response to treatment

LONG-TERM PERIOD
TARGET ALCOHOL BEHAVIOR

SHORT-TERM PERIOD
TARGET LIVER INJURY

Long-term outcome depend more on alcohol relapse then response to corticosteroids

Same is true in non-hepatic diseases: beneficial effect of tight control of blood pressure disappeared in the long-term when no strategy to maintain such control was made

Corticosteroids in severe alcoholic hepatitis: Not a Ferrari, but way better than walking...