Background

- 40-60% of patients with severe alcoholic hepatitis (SAH) die within a few months of diagnosis. (1)
- Since 1971, the treatment of SAH has generated much controversy, with many clinical trials and meta-analyses having inconsistent results.
- We specifically reviewed if prednisolone or prednisone improves the survival of patients with SAH at four weeks.

Methodology

- This review was done according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. (fig.1)
- PubMed, Embase, Ovid, Web of Science, and Cochrane Library were comprehensively searched from inception of these databases to June 2022.
- Search string was: (severe alcoholic hepatitis) AND ((prednisolone) OR (prednisone)).
- Pre-specified primary endpoint was all-cause mortality within 4 weeks of starting prednisolone or prednisone.
- Using DerSimonian and Laird method, Random-effects model meta-analysis via Cochrane RevMan 5.4 statistical software was performed on extracted data. (2)
- Statistical significance level was set at 0.05 with confidence interval calculated at 95%.
- Heterogeneity was assessed with Higgins I², and funnel plot was used to assess for publication bias. (3)
- Risk of Bias -2 (RoB-2) tool was used to evaluate the biases of each included randomized controlled trial (RCT). (4)

Results

- Out of 443 studies, 9 studies (8 RCTs and 1 retrospective study) including 920 patients were included in the meta-analysis.
- Mean age of participants was 48.1 ± 9.5 years, male to female ratio was 1.55 : 1.
- Oral prednisolone 40mg/day was administered for at least 2 weeks in 8 of the 9 studies.
- On pooled multivariate analysis, there was no statistically significant difference in the short-term mortality rate between the steroid-treated group and placebo-treated group (OR: 0.66, 95% CI: 0.42 - 1.02, p: 0.06, I²: 21%).

Discussion

- Corticosteroid interventions in the included studies varied regarding dosing style and duration.
- Our meta-analyses showed that corticosteroid, in comparison to placebo, did not show significant benefit in reducing all-cause mortality rate at one month in patients with SAH.
- However, because the confidence interval of the effect estimate only slightly cross the statistical significance threshold, we cannot exclude the possibility of a short-term beneficial effect in some sub-group of patients.
- Although current body of evidence does not show a reduction in short-term all-cause mortality rate in steroid treated group compared to placebo. Further larger scale RCTs and sub-group sensitivity analyses are still needed on this topic.

Conclusion and Recommendation

- Prednisolone/prednisone does not improve short-term survival in patients with severe alcoholic hepatitis.
- Future studies should explore sub-group sensitivity analyses.

References

2) Review Manager [RevMan] [Computer program]. Version 5.4. The Cochrane Collaboration, 2020

Disclosure

- All authors declare that they have no conflicts of interest.