20W114

Predictors of treatment response to interferon in chronic hepatitis B

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Introduction

Hepatitis B virus (HBV) is a double-stranded DNA virus with a variety of modes of transmission. Despite many countries implementing vaccination programs against the virus, it remains an important health problem worldwide. There are estimated 250 million HBV carriers in the world. Approximately 600,000 die annually from HBV-related liver disease[1].

Decision to commence treatment of the disease is based on presence or absence of cirrhosis, the ALT level, and the HBV DNA level. There are two main branches of treatment currently; pegylated Interferon and the nucleoside analogues, tenofovir and entecavir.

Interferon is a subcutaneous injection (usually 180mcg) given weekly for 48 weeks. Nucleoside analogues are oral medications which have no established optimum duration. The benefits of Interferon treatment are limited duration of treatment, cost reduction in comparison with lifelong nucleoside analogues

Aims

We planned to determine the outcomes of treatment for HBV and recognise criteria that would identify suitable patients to start on Interferon treatment.

By recognising criteria for treatment futility we could identify patient in which interferon would not be effective, thus avoiding exposing these patients to side effects.

Methods

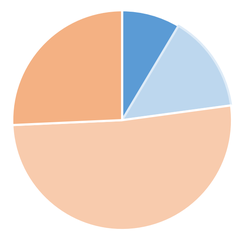
An observational retrospective cohort study was undertaken. We identified 35 patients who were treated with Interferon from 2005-2019 in the Liver Centre in MMUH. The medical charts of these patients were analysed for the below criteria.

Disease Variables	Treatment Variables
❖Gender	❖Treatment duration
❖Nationality	❖Final treatment dose
❖Genotype	❖eAg at start and end of treatment
❖Pre-treatment biopsy	❖sAg at start and end of treatment
❖Pre-treatment fibroscan	❖Viral load at start, weeks 12, 24, end of treatment
	❖ALT at start, weeks 12, 24, end of treatment

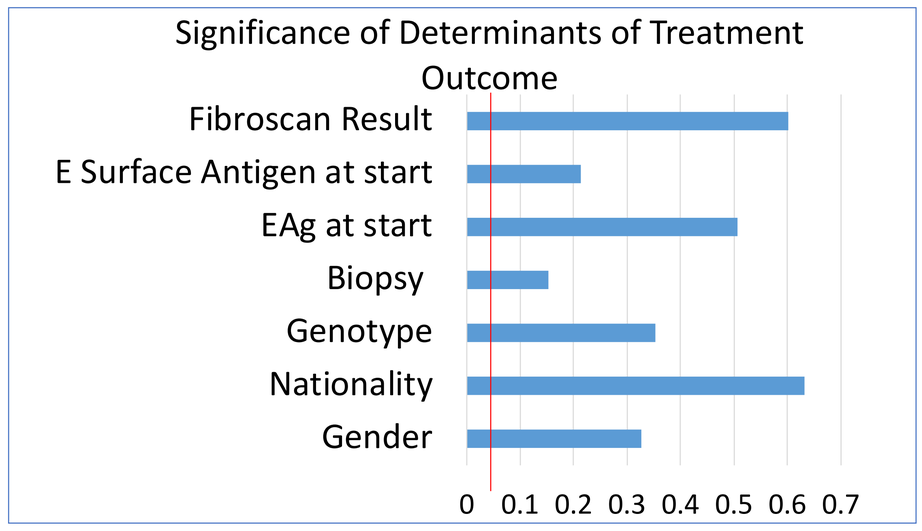
Patients were divided into two groups; positive and negative response. A positive response was defined as a sustained virological response and/or eAg seroconversion to eAb. A negative response was defined as cases where this was not achieved. Null responders were the negative group. Cases were excluded if treatment was not completed due to poorly tolerated side effects. Data was analysed using SPSS.

Results

A total of 35 patients were included in the database. Mean age was 35.17 years. EAg seroconversion and SVR (blue) were analysed together as a positive response. Null response and other (orange) were grouped as negative. Successful treatment was seen in 30.7% of our cohort.



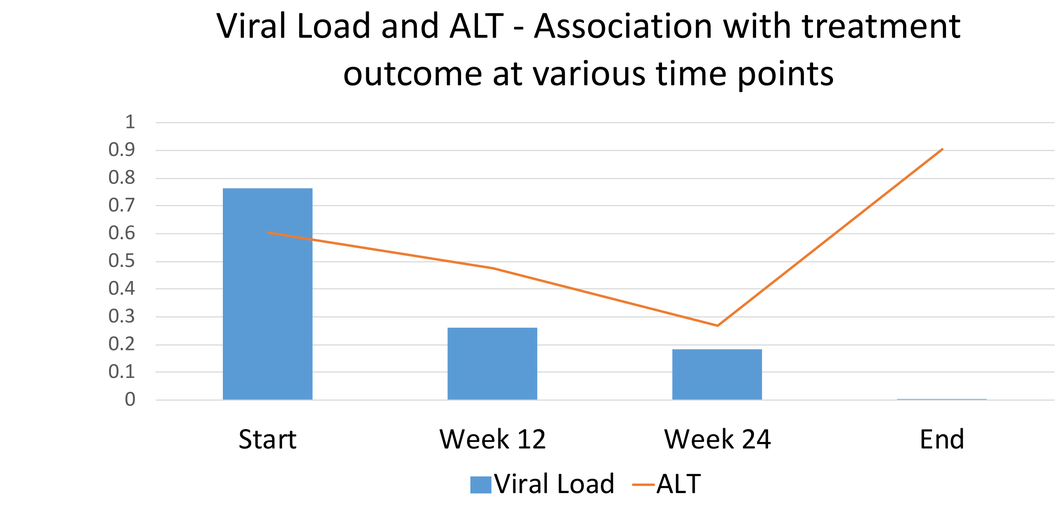
Results



Chi Square Test did not find any significant associations between chosen variables and positive outcome, which was the primary aim.

Friedman Test was completed to analyse whether there is a significant change in viral load across the 4 time points for whole cohort and then specifically for treatment positive versus negative, this was found to be significant (p=0.01). The same test was completed for ALT which found that there was a significant decrease in patient's with positive outcomes, however not negative outcomes. This indicates that a lack of decrease in ALT could be an early indicator that the treatment is not successful.

Mann Whitney U- Test showed that ALT at any time point cannot determine treatment outcome. Viral load at end is only determinant, as expected.



Conclusion

Treatment with Interferon was successful in 30.7% of the cohort. There are no significant associations between any of the variables we analysed and treatment outcome.

ALT and viral load levels taken at various points throughout treatment were analysed. It was demonstrated that these values could not determine whether the treatment would be successful at any time point other than at treatment end.

Viral load was the only significant indicator of treatment outcome, as expected. ALT in the negative treatment cohort did not decrease over time as in other group.

Unfortunately we were working with a small sample size, unclear if could translate to larger scale.

This study shows there is a low but definite response to interferon treatment in our patients with chronic hepatitis B. With no predictive factors, this figure can be used to counsel patients prior to therapy.

References

1. Razavi-Shearer D, Gamkrelidze I, Nguyen M, Chen D, Van Damme P, Abbas Z et al. Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study. The Lancet Gastroenterology & Hepatology. 2018;3(6):383-403.