

Letter to the Editor

COMMENT ON: ASSESSMENT AND MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

Wai Desmond. Assessment and Management of Non-alcoholic Fatty Liver Disease. Singapore Family Physician. 2019;45(2) 19-21

Dear Editor,

In his article, Dr Wai provided an enlightening summary and an insightful discussion of the assessment and management of Non-Alcoholic Fatty Liver Disease (NAFLD). The author alluded to the growing burden of the disease in the local landscape based on small cohort studies. This is unsurprising and to be expected with the emergence of highly potent and effective anti-viral medications such as Nucleos(t)ide Analogues (NA) for Hepatitis B and Direct Anti-Viral Agents (DAAs) for Hepatitis C, as well as the rising prevalence of obesity and metabolic risk factors such as diabetes mellitus, hypertension and hyperlipidemia locally leading to NAFLD and Non-Alcoholic Steatohepatitis (NASH).

As NAFLD/NASH will probably overtake viral hepatitis as the leading causes of chronic liver disease, cirrhosis and hepatocellular carcinoma in the future both locally and globally, the primary care physician is expected to play an integral role in the competent assessment and management of NAFLD.

Dr Wai suggested Pioglitazone and Vitamin E as part of the pharmacological options available for NASH. It is necessary for primary care physicians to be aware that the majority of internationally recognized guidelines including the American Association of Liver Disease (AASLD)¹ and the European Association for the Study of the Liver (EASL)² recommend only biopsy-proven NASH for pharmacological treatment.

In addition to the risk of heart failure, the United States Food and Drug Administration (FDA) also warned of an increased risk of bladder cancer with Pioglitazone. It is also noteworthy that in the landmark Pioglitazone, Vitamin E or Placebo for Nonalcoholic Steatohepatitis (PIVENS) study³, biochemical resolution was not observed in the PIVENS study (biochemical response is an unreliable predictor of efficacy) even though histological improvement was seen. In addition, in the Effect of Vitamin E or Metformin for Treatment of Nonalcoholic Fatty Liver Disease in Children and Adolescents (TONIC) study⁴, biochemical resolution was not sustained after treatment cessation. It is also important to note that both studies were conducted for only 96 weeks, and Vitamin E should also not be started in diabetic patients.

Almost all NAFLD/NASH patients seen at the primary care setting are diagnosed based on circumstantial clinical, biochemical and radiological evidence, and in the absence of a liver biopsy. It must also be pointed out that pharmacological treatment has not been proven superior to lifestyle modification. Therefore, the treatment with the best evidence for NAFLD remains non-pharmacological, i.e. exercise and hypocaloric diet leading to weight loss.

I also wish to particularly caution against the unnecessary cessation of statin therapy in NAFLD/NASH patients. Statin is generally safe and confers beneficial cardiovascular effects in this group of high cardiovascular risk patients as we know from the Greek Atorvastatin and Coronary Heart Disease Evaluation (GREACE) study.⁵

NAFLD/NASH represents the tip of the global metabolic pandemic. All primary care physicians, both in public and private practice, should receive adequate funding and support to stem the rising tide of the cardiovascular morbidity and mortality. This preventive and pre-emptive strategy is likely to be cost-effective in the long run.

Thank you for the consideration of the publication of this letter in your esteemed journal.

Yours sincerely,

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Letter to the Editor

AUTHOR'S REPLY:

Dear Editor,

I will like to thank Dr Poh for taking note of my article and giving his comment to the journal.

I fully agree with Dr Poh that non-alcoholic fatty liver disease (NAFLD) has become the most important liver disease worldwide, including Singapore. And NAFLD will become the leading cause for hepatocellular carcinoma, liver failure and liver cirrhosis.

Dr Poh pointed out that the current treatment for NAFLD are only recommended on biopsy-proven non-alcoholic steatohepatitis (NASH). Biopsy is currently the gold standard in diagnosis and staging of NASH. Most hepatologists could only conduct therapeutic studies on NASH or NAFLD patients after biopsy confirmation. Hence, it is not surprising that pioglitazone and vitamin E are recommended in biopsy-proven patients.

As a matter of fact, all therapeutic trials on viral hepatitis B and C are conducted in patients with biopsy-proven disease.

Though liver biopsy is not a routine investigation in clinical practice, biopsy is likely to remain as the entry criteria investigations in majority of hepatology related studies.

Dr Poh has rightly pointed out the numerous adverse effects of pioglitazone and vitamin E, which I have also highlighted in my original article and my lecture in January 2019. One important lesson from these therapeutic trials is that even if a particular treatment works for NASH or NAFLD, the benefit would wean off once the therapy is stopped.

It is likely that any future therapeutic agents would need to be consumed for many years, which will also bring up significant adverse effects.

I did not mention statin in the article, as statin per se, have no direct benefit on NAFLD or NASH. The common clinical difficulty primary care physicians often face is elevated liver enzymes after a patient with dyslipidemia and NAFLD is started on a statin. The physician would then have to differentiate if the hepatitis is caused by statin, or caused by underlying NAFLD.

As NAFLD is common among patients with dyslipidemia, I would recommend checking a baseline liver function test before starting statin, so as to set as a baseline for future comparison.

Lastly, I fully agree with Dr Poh that more local studies on NAFLD, especially from primary care setting, are urgently needed to help answer all the unknowns on NAFLD in Singapore.

Yours sincerely,

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