Non-alcoholic fatty liver disease: the important role for primary care

Welcome to this second electronic issue of *Diabetes & Primary Care* journal.

Non-alcoholic fatty liver disease

This week, I saw three people with newly diagnosed non-alcoholic fatty liver disease (NAFLD) – two of them with type 2 diabetes – prompting me to review recent guidelines and to assess how we manage all aspects of NAFLD.

Liver steatosis in those without significant alcohol intake (NAFL), with its potential progression to non-alcoholic steatohepatitis (NASH) with liver injury and fibrosis/cirrhosis, seems set to overtake alcohol and hepatitis as the most common cause of liver failure and need for transplantation over the next decade. Seeing three new cases in one week prompted me to question how common it is.

Prevalence figures are difficult to assess as many people remain undiagnosed. However, it is estimated that 17–46% of people eating a Western diet have some degree of NAFLD (European Association for the Study of the Liver [EASL] et al, 2016), with those with insulin resistance and type 2 diabetes particularly affected, while 2–5% have NASH with liver injury and 1–2% may be at risk of progressing to cirrhosis (Neuschwander-Tetri, 2017).

Any degree of fibrosis is the most important predictor of adverse outcomes, while type 2 diabetes, obesity and older age are associated with NASH development and progression. A review in *BMC Medicine* (Neuschwander-Tetri, 2017) nicely summarises the substrate overload lipotoxic liver injury (SOLLI) model of NASH, reminding us that excess dietary sugars trigger fatty acid production in the liver (*de novo* lipogenesis; DNL) and that this, together with fatty acids released from adipose tissue, raises the level of liver free fatty acids. If these cannot be rapidly utilised or transported out of the liver, they may divert into pathways producing lipotoxic lipids that cause hepatocellular injury, inflammation and NASH. Diverse factors such as hypoxia/obstructive sleep apnoea (OSA), elevated uric acid and gut microbiome changes (resulting in endogenous alcohol production) may potentiate liver injury.

Some papers suggest an important role for dietary fructose (DiNicolantonio et al, 2017), as one of my patients highlighted. This passes directly to the liver for metabolism, where it has a significant impact on stimulating DNL and other actions that may increase NAFLD/NASH risk. It is difficult to separate the effects of calories and specific dietary components, although high-calorie diets, excess saturated fat, refined carbohydrates and sugar-sweetened beverages (SSBs) have been cited as contributing factors (EASL et al, 2016). One small, short-term study concluded that replacing SSBs high in fructose with artificially sweetened beverages (ASBs) decreased intrahepatic fat over 12 weeks in overweight people with high SSB consumption (Campos et al, 2015). Many studies are US-based, where SSBs contain high fructose corn syrup, whereas in the UK the sweetener is sucrose (digested to 50% glucose, 50% fructose). Coca-Cola Classic contains 139 kcal and 35 g (7 teaspoons) sucrose per 330-mL can compared to 1 kcal and no sucrose in the Diet and Zero versions. However, ASBs may have other adverse effects.

Human dietary intervention studies are small, of short duration and often use excessive additional calories or extremes of macronutrient dietary manipulation that do not reflect real-life consumption. More research is, therefore, urgently needed on dietary factors contributing to pathogenesis or management of NAFLD.

So, what is our role? When sharing the diagnosis of NAFLD from an ultrasound scan, we can encourage lifestyle modification with reductions in calorie, fructose and sugar consumption, and adoption of a Mediterranean diet. Follow up to motivate gradual weight loss (including consideration of orlistat) and encouragement of regular exercise are the mainstays of treatment. Alcohol increases risk of progression, so careful history-taking and appropriate advice are important.

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Citation: Brown P (2018) Non-alcoholic fatty liver disease: the important role for primary care. *Diabetes & Primary Care* **20**: 87–8

"NAFLD is a developing and important disease in adults and children with and without diabetes, and many controversies remain."

An active search for NASH in those at highest risk (including those over 50 or with type 2 diabetes) requires referral for imaging and biopsy. Bariatric surgery, when accessible, may reverse NASH. There are currently no drugs licensed for NASH, although pioglitazone has been shown to be beneficial in those with (Cusi et al, 2016) and without (Sanyal et al, 2010) diabetes, and the small LEAN trial (Armstrong et al, 2016) using liraglutide demonstrated benefit. Hepatocellular carcinoma may supervene in those with NASH even before cirrhosis develops, so encouraging attendance for surveillance is important.

This is a developing and important disease in adults and children with and without diabetes, and many controversies remain. Later this year, our "How to diagnose and manage NAFLD" will provide a concise summary for primary care teams. In the meantime, I believe that, based on the proposed pathogenesis discussed here, we have a responsibility to help people, including the parents of obese children, understand the importance of lifestyle changes in seeking to reduce this potential epidemic of liver disease. Prevention or reversal of liver fat accumulation in the early stages will be more impactful than intervening once liver damage has developed, and lifestyle interventions will have added benefit in control of the often coexisting diabetes. I believe it is time we all gave some thought to how we can help people defend themselves against this latest lifestyle-induced challenge.

In this issue

Nicola Milne and I share important news stories from the American Diabetes Association conference and other news in brief.

Colin Kenny leads us through the important hypertension papers that have led to our current blood pressure targets and management options, while Jane Diggle continues our useful series with "How to diagnose and manage hypertension in diabetes". As with all the "How to…" resources, you can download the PDF and print and pin it up in your consulting room (**http://bit.ly/2Lp9w0h**).

Up to 48% of people with type 2 diabetes may have OSA (Einhorn et al, 2007). Following on from his comment piece in our last issue (**http://bit.ly/2udUnmQ**), Matt Capehorn summarises how we can identify those with OSA, and play our role in reducing the significant morbidity and mortality associated with undiagnosed OSA.

Olga Kozlowska and Rustam Rea have reviewed examples of diabetes enhanced services around the UK and highlight the paucity of outcome data collated or published that might have informed decision-making about what should be incentivised going forward. I provide an update on the inequalities of enhanced service funding and resulting demotivation amongst primary care teams in parts of Wales.

The Primary Care Diabetes Society (PCDS) is surveying the knowledge, skills and funding for diabetes care delivery across England, Northern Ireland, Scotland and Wales. The results will be collated into *The State of the Nations* report, which will be launched in Westminster in October this year. I hope that as many of you as possible will complete the short survey by following this link: **http://bit.ly/2nC8YG3**. Some of you will also have received an email containing the link, with more detail on how your anonymised responses will be used. As a society, we need to understand what limits care delivery and where the gaps in knowledge and care are, so this can inform the society's education and policy work, and allow us to lobby for improved patient care more effectively.

Here in Wales, 100% of practices have been contributing data to the National Diabetes Audit (NDA) for a few years, and the real-time data this provides is useful for benchmarking care delivery. Roger Gadsby's comment outlines the significant changes to the NDA that we can expect over the next cycle.

Victoria Ruszala highlights the important role of pharmacists in diabetes care and the launch of *An Integrated Career and Competency Framework for Pharmacists in Diabetes*, based on the TREND competencies framework for nurses.

Finally, our featured Welsh Assembly-funded CPD module helps improve our accuracy in diagnosis of diabetes. Review the questions in our module flier to see whether you and your team could benefit from the module.

I hope you find time to read and share this issue with your colleagues and that I have prompted discussion on how we choose to manage people with NAFLD. Enjoy the rest of your summer. ■

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