EASL Policy Statement on Food, obesity and Non-Alcoholic Fatty Liver Disease (NAFLD)

Executive Summary

Non-alcoholic fatty liver disease (NAFLD) affects approximately 1 in 4 members of the general population across Europe and so is a major health problem due to its high prevalence, capacity to progress to liver cirrhosis and liver cancer, and also because it is associated with a greater risk of cardiovascular disease & other malignancies. Policy interventions at population and individual levels are necessary in order to reduce the growing burden of liver disease arising due to NAFLD.

Aim

The aim of this European Association for the Study of the Liver (EASL) policy statement is to inform politicians, policy-makers and the general population across Europe about NAFLD and the measures required to prevent and treat this common progressive condition.

Main messages

1. NAFLD is a disease strongly linked with obesity, insulin resistance (diabetes and pre-diabetes), dyslipidaemia and hypertension: the “metabolic syndrome”.

2. NAFLD affects 1 in 4 people across the EU, with a prevalence varying markedly according to geography and across different socio-economic and ethnic groups. The prevalence of NAFLD continues to rise and it is now becoming one of the most frequent causes of cirrhosis (advanced liver disease) and liver transplantation in Europe.

3. NAFLD is strongly linked with unhealthy lifestyles. This is driven by excessive energy intake and an unhealthy diet, which is in part a consequence of advertising, increasing availability and low cost of industrially processed fast food and sugared sweetened beverages. Lack of physical activity is another significant contributor. This means that there is a great potential to treat or prevent NAFLD from developing, especially if at risk groups are effectively targeted for intervention.

4. Population level measures to promote lifestyle change have been shown to be effective at preventing obesity and encouraging weight loss, which has a well demonstrated efficacy in treating NAFLD.

5. Unless patients with NAFLD are identified and diagnosed, they are denied the knowledge and opportunity to make the necessary changes. It is important to identify, and risk stratify patients with NAFLD in order to implement therapeutic interventions.

Introduction

Non-alcoholic fatty liver disease (NAFLD), which represents the accumulation of excess fat in the liver, is now the commonest cause of liver disease in Western countries and reflects the rising levels of obesity and type 2 diabetes mellitus (T2DM)[1 2]. NAFLD refers to a spectrum of disease ranging from steatosis to steatohepatitis (NASH) and on to cirrhosis[3]. NAFLD affects about 25% of the population of Europe(1), with the prevalence and severity rising further in individuals that are overweight and/or have type 2 diabetes mellitus, reflecting its strong association with the metabolic syndrome. Patients with NAFLD have an increased risk of dying from liver disease, cardiovascular disease and most causes of cancer, with modeling suggesting that the annual predicted economic burden of NAFLD in Europe would be >€35 billion of direct costs and a further €200 billion of societal costs(2).

More than half of adults and one third of children in Europe are classified as overweight or obese[4], with the proportion being highest in those from lower socio-economic groups. Unhealthy behaviour, namely a lack of physical activity and excess calorie intake together with high consumption of fructose and saturated fats[5] (3-5)[6] leads to weight gain and/or ectopic fat deposition, which plays a major role in the development and progression of NAFLD[7]. Moreover, children and adolescents that are overweight are at greater risk of staying overweight as adults (6).

Across the WHO European Region, children are regularly exposed to marketing that promotes foods and drinks high in energy, saturated fats, trans-fatty acids, added sugar (meaning refined sugars: sucrose, fructose and high fructose corn syrup - HFCS incorporated into food and beverages[8]) or salt[9]. Such targeting of children/adolescents to food and beverage commercials, and in particular those embedded in children's TV programmes, electronic media, including video games, DVDs etc.[10] and social media such as Instagram and YouTube[11] have been demonstrated to drive consumption of high-calorie and low-nutrient beverages and foods. Of note, sugar-sweetened beverages (SSBs) are one of the largest sources of added sugar and an important contributor of calories with few, if any, other nutrients.[12] Consequently, consumption of SSBs is now one of the leading causes of childhood and adult obesity(7, 8), and is associated with NAFLD and increased liver damage (NASH and fibrosis) in NAFLD patients.[13 14 15 16 17]. Research indicates that governmental measures aimed at increasing the cost of SSBs can reduce consumption and decrease weight (9). In addition, saturated fat consumption increases liver fat, in contrast to healthier fats as mono and poly-unsaturated fats, such as in the Mediterranean diet which is beneficial in the treatment of NAFLD[18 19 20 21], characterized by a high intake of olive oil, nuts, fruits & vegetables, legumes and fish and a low intake of red and processed meat, and added sugar.

Lack of physical activity and increasing sedentary behavior are becoming a growing concern in both children and adults, resulting in excessive adiposity and type-2 diabetes. Physical activity, both aerobic and resistance training, produces significant changes in liver fat,[22 23 24] which, along with the strong cardiovascular benefits, make it an essential adjunct to healthy eating. Just as the marketing environment influences eating behaviour, the built environment influences physical activity. Establishment of a safe and appealing walking and cycling infrastructure can have a major influence on behaviour, with the recent World Health Organisation Global Action Plan on Physical Activity (10) providing a framework to support policy and practice in this area.

Measures to target obesity will have a major beneficial effect in preventing the development of NAFLD and its complications, but will require concerted efforts if they are to be successful. A WHO meta-review of 11 recent systematic reviews on the effectiveness of fiscal policies to reduce weight, improve diet and prevent chronic diseases (noncommunicable diseases) concluded that the strongest evidence to date was for SSBs levies, reducing consumption by 20-50% (9). A recent study, modeled on a 20% levy on SSB in the UK, estimated that it would prevent 3.7 million cases of obesity and 25,498 cases of BMI-related disease over the next 10 years (2015-2025), thus avoiding £10million in National Health Service costs in 2025 alone (11).

Such approaches will also be important in the treatment of patients with NAFLD[25], especially given the absence of any licensed pharmacological therapies at present. One of the additional challenges is the lack of awareness amongst policy-makers, the public and primary care doctors that obesity and T2DM can lead to significant liver disease. This is made worse by the lack of good biomarkers to identify which patients have developed NAFLD, and which have progressed to more advanced disease, namely NASH.

The implementation of a "multidisciplinary team approach" in which patients will be supported by physicians, endocrinologists and dietitians/nutritionists is recommended[26] , with one of the team's roles being to act as a catalyst for behavioural change by improving the patients' motivation to adopt and maintain diet and physical activity recommendations.

Conclusions and recommendations

Prevention and treatment of NAFLD

A principal focus is to address obesity in Europe which will then impact on the levels of NAFLD. Measures include:

- Promoting local infrastructure changes that encourage physical activity.
- Promoting water consumption instead of SSBs by making drinking water easily accessible to children and adults in public facilities including parks, playgrounds, schools, and worksites.
- Promoting population-based policies to restrict advertising and marketing of SSBs and industrially processed foods high in saturated fat, sugar and salt to children.
- Implementing fiscal measures for SSBs, as well as implementing fruit and vegetables subsidies.
- Using legislation to ensure that the food industry improves the composition (reformulation) of processed foods (e.g. reducing trans and saturated fat, sugar and salt content).
- Mandating nutritional labeling, in particular "traffic light labeling", as well as labeling of calories on menus of fast food restaurants.

Targets for NAFLD

- Disseminating the message that liver disease can occur from causes other than too much alcohol.
- Educating the public on what NAFLD is and what it means for their future health, by explaining the higher risk for further liver complications, including chronic liver disease, liver cirrhosis and HCC (liver cancer). Ensuring these messages are conveyed to policymakers and politicians.

- Educating primary care practitioners on the high prevalence of NAFLD in the general population and the potential liver-related morbidities, emphasizing the importance of case-finding for NASH in high risk groups such as those that are overweight/obese and diabetic.
- Expanding the knowledge and skills of medical care providers about the potential risk factors linked to NAFLD, how to conduct nutrition screening and counseling and create a network of specialists (e.g. nutritionists) to properly address this issue.
- Establishing clinical networks between general practitioners, endocrinologists, cardiologists, nutritionists and hepatologists in order to provide a comprehensive management of cardio-metabolic and hepatic comorbidities.
- Emphasizing the benefits of diets such as the Mediterranean diet that can reduce liver fat even without weight loss and prevent cardiovascular disease and diabetes.
- Strongly encouraging regular moderate to vigorous physical activity (according to the patient's ability), by both aerobic and resistance training, as this can produce significant changes in liver fat. Target a reversal of sedentary behavior, in addition to physical activity and exercise guidelines.
- Engaging patients in appropriate strategies for behavioural modification to avoid relapse and weight regain.

References

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global Epidemiology of Non-Alcoholic Fatty Liver Disease-Meta-Analytic Assessment of Prevalence, Incidence and Outcomes. Hepatology. 2015.
2. Younossi ZM, Blissett D, Blissett R, Henry L, Stepanova M, Younossi Y, et al. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. Hepatology. 2016;64(5):1577-86.
3. Zelber-Sagi S, Ratziu V, Oren R. Nutrition and physical activity in NAFLD: an overview of the epidemiological evidence. World journal of gastroenterology. 2011;17(29):3377-89.
4. Miele L, Dall'armi V, Cefalo C, Nedovic B, Arzani D, Amore R, et al. A case-control study on the effect of metabolic gene polymorphisms, nutrition, and their interaction on the risk of non-alcoholic fatty liver disease. Genes Nutr. 2014;9(2):383.
5. Romero-Gomez M, Zelber-Sagi S, Trenell M. Treatment of NAFLD with diet, physical activity and exercise. J Hepatol. 2017;67(4):829-46.
6. Freedman DS, Khan LK, Serdula MK, Dietz WH, Srinivasan SR, Berenson GS. The relation of childhood BMI to adult adiposity: the Bogalusa Heart Study. Pediatrics. 2005;115(1):22-7.
7. Johnson RK, Appel LJ, Brands M, Howard BV, Lefevre M, Lustig RH, et al. Dietary sugars intake and cardiovascular health: a scientific statement from the American Heart Association. Circulation. 2009;120(11):1011-20.
8. Dhingra R, Sullivan L, Jacques PF, Wang TJ, Fox CS, Meigs JB, et al. Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. Circulation. 2007;116(5):480-8.
9. World Health Organization. Fiscal policies for diet and prevention of noncommunicable diseases: technical meeting report, 5-6 May 2015, Geneva, Switzerland. 2016. .
10. Global action plan on physical activity 2018–2030: more active people for a healthier world. WHO, Geneva 2018. ISBN: 978-92-4-151418-7. http://www.who.int/ncds/prevention/physical-activity/global-action-plan-2018-2030/en/.
11. Cancer Research UK, UK Health Forum. Short and sweet: why the government should introduce a sugary drinks tax. 2016.

Further references

[1] Younossi ZM, Blissett D, Blissett R, et al. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. Hepatology 2016; 64:1577-1586.
[2] Younossi ZM, Koenig AB, Abdelatif D, et al. Global Epidemiology of Non-Alcoholic Fatty Liver Disease-Meta-Analytic Assessment of Prevalence, Incidence and Outcomes. Hepatology 2015.
[3] Townsend SA, Newsome PN. Review article: new treatments in non-alcoholic fatty liver disease. Aliment Pharmacol Ther 2017;46:494-507.
[4] http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity/data-and-statistics.
[5] Zelber-Sagi S, Ratziu V, Oren R. Nutrition and physical activity in NAFLD: an overview of the epidemiological evidence. World J Gastroenterol 2011;17:3377-89.
[6] Romero-Gomez M, Zelber-Sagi S, Trenell M. Treatment of NAFLD with diet, physical activity and exercise. J Hepatol 2017; 67:829-846.
[7] European Association for the Study of the L, European Association for the Study of D, European Association for the Study of O. EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol 2016; 64:1388-402.
[8] Howard BV, Wylie-Rosett J. Sugar and cardiovascular disease: A statement for healthcare professionals from the Committee on Nutrition of the Council on Nutrition, Physical Activity, and Metabolism of the American Heart Association. Circulation 2002;106:523-7.
[9] Health inequalities in the EU — Final report of a consortium. Consortium lead: Sir Michael Marmot. 2013.
[10] Institute of Medicine, Food marketing to children and youth: threat or opportunity? Washington, D.C., The National Academies Press. 2006.

[11] Boyland E, Tatlow-Golden, M: Exposure, power and impact of food marketing on children: Evidence supports strong restrictions; European Journal of Risk Regulation, 2017, 8 (02). 224 - 236. ISSN 1867-299X, 2190-8249
[12] The CDC Guide to Strategies for Reducing the Consumption of Sugar-Sweetened Beverages. 2010.
[13] Zelber-Sagi S, Nitzan-Kaluski D, Goldsmith R, et al. Long-term nutritional intake and the risk for non-alcoholic fatty liver disease (NAFLD): a population-based study. J Hepatol 2007 ;47 :711-7.
[14] Ma J, Fox CS, Jacques PF, et al. Sugar-sweetened beverage, diet soda, and fatty liver disease in the Framingham Heart Study cohorts. J Hepatol 2015;63:462-9.
[15] Abdelmalek MF, Suzuki A, Guy C, et al. Increased fructose consumption is associated with fibrosis severity in patients with nonalcoholic fatty liver disease. Hepatology 2010; 51:1961-71.
[16] Maersk M, Belza A, Stodkilde-Jorgensen H, et al. Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study. Am J Clin Nutr 2012;95:283-9.
[17] Mosca A, Nobili V, De Vito R, et al. Serum uric acid concentrations and fructose consumption are independently associated with NASH in children and adolescents. J Hepatol 2017;66:1031-1036.
[18] Bozzetto L, Prinster A, Annuzzi G, et al. Liver fat is reduced by an isoenergetic MUFA diet in a controlled randomized study in type 2 diabetic patients. Diabetes Care 2012 ;35 :1429-35.
[19] Ryan MC, Itsiopoulos C, Thodis T, et al. The Mediterranean diet improves hepatic steatosis and insulin sensitivity in individuals with non-alcoholic fatty liver disease. J Hepatol 2013;59:138-43.
[20] Rosqvist F, Iggman D, Kullberg J, et al. Overfeeding polyunsaturated and saturated fat causes distinct effects on liver and visceral fat accumulation in humans. Diabetes 2014; 63:2356-68.
[21] Bjermo H, Iggman D, Kullberg J, et al. Effects of n-6 PUFAs compared with SFAs on liver fat, lipoproteins, and inflammation in abdominal obesity: a randomized controlled trial. Am J Clin Nutr 2012;95:1003-12.
[22] Hashida R, Kawaguchi T, Bekki M, et al. Aerobic vs. resistance exercise in non-alcoholic fatty liver disease: A systematic review. J Hepatol 2017;66:142-152.
[23] Thoma C, Day CP, Trenell MI. Lifestyle interventions for the treatment of non-alcoholic fatty liver disease in adults: a systematic review. J Hepatol 2012; 56:255-66.
[24] Keating SE, Hackett DA, George J, et al. Exercise and non-alcoholic fatty liver disease: a systematic review and meta-analysis. J Hepatol 2012;57:157-66.
[25] Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight Loss Through Lifestyle Modification Significantly Reduces Features of Nonalcoholic Steatohepatitis. Gastroenterology 2015;149:367-78 e5; quiz e14-5.
[26] Bellentani S, Dalle Grave R, Suppini A, et al. Behavior therapy for nonalcoholic fatty liver disease: The need for a multidisciplinary approach. Hepatology 2008;47:746-54.

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