

Nonalcoholic Fatty Liver Disease and Steatohepatitis: Pharmacotherapeutic Trends

Novy Gupte^{1*} and Suraj Gupte²

¹Department of Pharmacology, Lady Hardinge Medical College, New Delhi, India

²Postgraduate Department of Pediatrics, Mamata Medical College and Hospitals, Khammam, Telangana, India

***Corresponding Author:** Novy Gupte, Department of Pharmacology, Lady Hardinge Medical College, New Delhi, India.

Received: March 24, 2017; **Published:** May 05, 2017

The relatively newly-recognized entity, nonalcoholic fatty liver disease (NAFLD), is defined by liver fat deposition in the absence of excessive alcohol intake. It is the most common cause of chronic liver disease in children, more so obese ones. It has attained epidemic proportions during the past couple of decades as a consequence of spurt of paediatric overweight and obesity not only in the prosperous countries but also resource-limited countries including India [1].

NAFLD is strongly associated with metabolic syndrome, a cluster of increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels occurring together. There is a growing evidence that it enhances the risk for future cardiovascular disease, stroke and diabetes mellitus.

Nonalcoholic steatohepatitis (NASH), a progressive form of NAFLD, first described in 1983, invariably ends up with advanced hepatic fibrosis, cirrhosis and death. With increasing incidence of obesity, NAFLD and NASH appear to be heading as a significant public health problem.

Genetic background, intrauterine environment and erratic postnatal nutrition have emerged as the major risk factors for development and progression of NAFLD and NASH.

Though firm diagnosis needs a liver biopsy (gold standard), non-invasive methods are good enough for screening.

Awareness of NAFLD and NASH is critical for adequate recognition and treatment of this potentially deadly disease. The sheet-anchor of treatment is multi-targeted therapeutic approach. Treatment should not only address the liver disease itself but also the comorbidities to improve the overall survival and quality of life (QOL) Nonpharmacological therapy revolves around lifestyle interventions aimed at weight loss through exercises and diet control. Bariatric surgery may be considered in select cases.

Currently, randomized-controlled trials are underway in the paediatric population to define pharmacological therapy for NAFLD and NASH [2]. Pharmacological interventions involve the use of medications to treat associated metabolic disorders, particularly insulin resistance, and use of antioxidants such as vitamins C and E as hepatoprotective agents [3].

Medications targeting insulin resistance include insulin-sensitizers, namely metformin and thiazolidinediones, statins, pentoxifylline, etc. Quite a few studies have demonstrated the improvement in histological changes from baseline liver biopsy following metformin therapy along with life style modifications.

In a study, children with biopsy proven NAFLD received Vitamin E, vitamin C, and ursodeoxycholic acid (UDCA) as potentially hepatoprotective agents, or placebo. An end-of-treatment, liver biopsy was done to assess histological changes [4]. There was convincing evidence of slowing down the progression of steatosis to steatohepatitis and other metabolic abnormalities associated with NAFLD and NASH by reduction of oxidative damage in the hepatoprotective group.

Statins, the lipid-reducing agents, ameliorate surrogate markers of steatosis as well as reduce the cardiovascular risks. Further well-planned studies are warranted to evaluate their impact on liver histology.

Hamid has carried out an extensive review of literature on evolving therapeutics in NASH [5]. Though encouraging response to such agents as anti-TNF α , angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARB) has been reported, in between there are documentations of results that are just equivalent to placebo effect.

Apparently, though several pharmacological agents have been used to treat NAFLD/NASH, most of the studies are of small size and of short duration. Well planned clinical trials for NASH need to target specific pathogenic pathways with an acceptable sample size and duration.

To sum up, undoubtedly, public health awareness and intervention are needed to promote healthy diet, exercise, and lifestyle modifications to prevent and reduce the burden of NAFLD in the community. Also needed is work for determining non-invasive biomarkers to identify children and adolescents with NAFLD. Equally significant are the initiatives for targeted pharmacological therapies to improve liver function and histology. These medications should be safe, cost-effective and readily available.

Bibliography

1. Mohan N and Sharma A. "Nonalcoholic fatty liver and steatohepatitis". In: Gupte S, Gupte SB, Gupte M (eds): Recent Advances in Pediatrics-22 Hot Topics. New Delhi: Jaypee (2014): 141-152.
2. Loomba R., *et al.* "Advances in pediatric nonalcoholic fatty liver disease". *Hepatology* 50.4 (2009): 1282-1293.
3. Giovanni M and Salvatore RD. "Antioxidant Therapy and Drugs Interfering with Lipid Metabolism: Could They Be Effective in NAFLD Patients?" *Current Pharmaceutical Design* 19.29 (2013): 5297-5313.
4. Wilson E and Smith AE. "Antioxidants in NAFLD and NASH". *Eur Med J* (2015): 145-151.
5. Hamid A. "Evolving trends in therapeutics of liver disease in children". *Asian Bulletin Therapeutics* 4 (2016): 125-134.

Volume 4 Issue 1 May 2017

© All rights reserved by Novy Gupte and Suraj Gupte.