Advancements in Saroglitazar Treatment for Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis: A Comprehensive Update

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Abstract:
Non-alcoholic fatty liver disease (NAFLD) is rapidly becoming one among the most important prevalent the reasons for persistent liver damage on a universal scale. Saroglitazar, an emerging dual PPAR ϑ/γ agonist, has a strong PPARα impact and a minor PPARγ action, while exhibiting few adverse reactions. This drug was approved by the DGCI in the year 2013. The medicine has been shown to be useful in the therapy of non-alcoholic fatty liver disease and non-alcoholic fatty liver disease in both animal and human investigations. Here we review the research works conducted national and international level regarding usage of the saroglitazer in the management of NASH or NAFLD. Saroglitazar is a prominent drug that can be used in the management of NASH and NAFLD. It offers less side effects and most effective in limiting the cumulation of fat in the liver also it improves the biochemical parameters. However, the clinical trials in this area are less and need to conduct more trials in multiple places to give more supportive data regarding use of the saroglitazer. The review recommends further translational research in this area.

Keywords: Saroglitazer, Liver diseases, Non alcoholic fatty liver, Fat accumulation, Dyslipidemia

Introduction:

Non-alcoholic fatty liver disease (NAFLD) has been shown to the predominant reason for chronic liver disease [1]. This is one of the important public health issues to be considered as the disease if untreated can progress to non-alcoholic steatohepatitis, cirrhosis or carcinoma. NAFLD is believed to be the hepatic component of diabetes mellitus. As it was observed that about 70-80 percentage of the patients of NAFLD are diabetic [2]. Also, the advancement of the illness in end-stage liver disease is caused by a gradual decrease of the capacity to regulate metabolism as a result of the physical modification associated with aging and dysbiosis of the gut [new ref]. Further, insulin resistance was reported to have a tremendous influence in the development of NAFLD by increasing liver's access to free fatty acids in the appropriate amounts [3]. Further if the inflammation is triggered, it leads to development of cirrhosis. Hence, the pharmacological agents that are developed to treat the NAFLD should prevent the fat deposition or the inflammation process [4]. The pharmacological agents that have promising effects are obeticholic acid and saroglitazar. These drugs have minimum side effects [5,6]. Peroxisome proliferator activated receptors (PPARs) are intracellular binding sites located within the cell nucleus and regulates the metabolic processes and growth and differentiation of the cells. The different forms of these receptors include alpha, beta, delta and gamma located in the liver, skeletal muscles and adipose tissues respectively [7]. Saroglitazar is a newly discovered compound that acts as a dual agonist for the PPARα and PPARγ receptors. It primarily activates the PPARα receptor, while also exerting a moderate effect on the PPARγ receptor. This compound has been found to have little negative impact. This drug was approved by the DGCI in the year 2013 [7]. Both animal and human studies affirm the potency of the drug in the regulation of NASH and NAFLD effectively [8-11]. Here we review the research works conducted national and international level regarding usage of the saroglitazer in the management of NASH or NAFLD.

Materials and methods:

A detailed review of literature from Pub Med, Google, and other online journals were reviewed using the search terms Saroglitazar, NAFLD, NASH.

International studies:

Earlier clinical trial reported that the administration of Saroglitazar 4 mg resulted in notable enhancements in alanine aminotransferase, liver fat content, glucose metabolism, and atherogenic dyslipidemia among individuals diagnosed with

NAFLD or NASH [14]. Another systematic review reported the possible drugs that can be effectively used to control non-alcoholic fatty liver are Semaglutide, obeticholic acid, firsocostat, cilofexor plus firsocostat and lubiprostone [15]. It was noticed that individuals who had undergone liver transplantation saw a significant drop in the amount of fat in their livers [19]. In this study the liver fat was evaluated using MRI proton density fat fraction. Archana Vijayakumar et al., reported that combination of drugs are more effective in the management of NASH [21]. Both animal and human studies reported that there was a significant improvement not only the biochemical parameters but also the histological parameters seen after the treatment with saroglitazer [22]. Zhuo-Ya Zhang et al., testified that the Saroglizatar is the medication that is the most successful in the treatment of NAFLD [25]. The group of drug that limits the build up of fat in liver and the consequent stress happens during metabolism include peroxisome proliferator-activator receptor agonists (eg, pioglitazone, elafibranor, saroglitazar) [27].

National studies:

In the yeonly new medication proposal for Saroglitazar that was submitted by Zydus Cadila has been approved (2020) for use in the treatment of NASH in India. The pathophysiology of the NASH is very complex. Hence a combination of drugs has to be used in the management [12]. Administration of Saroglitazar causes enahancement in transaminases, LSM, and CAP in NAFLD patients with diabetes dyslipidemia [13]. Observations indicating significant change in the cholesterol levels and glycemic parameters in the patients with diabetes. Further, no adverse effects were observed due to the usage of this drug [16]. People with liver disease showed a remarkable change of outcomes in the liver parameters and also improvement seen in triglycerides followed by treatment with saroglitazer [17]. Improvement in the liver parameters, metabolic parameters and reduction in the stiffness of liver was observed followed by administration of 4 mg of saroglitazar in NASH or NAFLD patients [18]. Sujit Chaudhuri et al., reported that the biochemical parameters had a substantial change and also significant reduction in the elastography parameters in patients with NAFLD [20]. Another research reported that saroglitazar improves transaminases and elastography in individuals with diabetic dyslipidemia and non-alcoholic fatty liver disease [23]. Another study by Mithun Sharma highlighted that there is a need for considering dietary modifications and weight reduction programs to the patients with NASH [24]. Animal study conducted by Suresh R Giri et al., reported that saroglitazar (1 and 3 mg/kg) administered to the animal models for 27 weeks cause significant reduction in the liver injury markers and also supressed the liver carcinoma [26]. Mukul R jain et al., testified that Saroglitazar, exhibited an inclusive development in NASH. Saroglitazar seems to have more favorable effects than fenofibrate and pioglitazone, which are both PPARα agonists, and pure PPARα agonists [28].

Conclusion:

Saroglitazar is a prominent drug that can be used in the management of NASH and NAFLD. It offers less side effects and most effective in limiting the pile up of fat in the liver also it improves the biochemical parameters. However, the clinical trials in this area are less and need to conduct more trials in multiple places to give more supportive data regarding use of the saroglitazer. The review recommends further translational research in this area.

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