

Original Article

Saroglitazar for non-obese metabolic-dysfunction associated steatotic liver disease (MASLD): An open-label randomised controlled trial

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Background and objectives: Nearly one-third of individuals with metabolic dysfunction-associated steatotic liver disease (MASLD)/non-alcoholic fatty liver disease (NAFLD) are non-obese, yet evidence for pharmacotherapy in this subgroup remains limited. This study assessed the safety and effectiveness of saroglitazar among non-obese individuals with MASLD/NAFLD.

Methods: In this open-label randomised controlled trial (RCT), non-obese [body mass index (BMI) <25 kg/m²] adults with NAFLD/MASLD and raised alanine aminotransferase levels (ALT >50 U/L) were allocated in a 1:1 ratio to either saroglitazar (4 mg/day) combined with lifestyle modification (Group A) or lifestyle intervention alone (Group B) for a period of six months. The trial was registered with clinical trial registry (CTRI/2022/09/046081). The primary outcome was the change in controlled attenuation parameter (CAP). Secondary outcomes included changes in anthropometric measures, insulin resistance, glycaemic indices, lipid profile, ALT, fibroscan-aspartate aminotransferase (FAST) score, hepatic steatosis index (HSI), non-invasive fibrosis markers [liver stiffness measurement (LSM), fibrosis-4 (FIB-4), aspartate aminotransferase to platelet ratio index (APRI)], and adverse events.

Results: Sixty-six participants (33 per group) completed the study. Both groups showed significant reductions in CAP; however, the median change in CAP did not differ between the two groups [24 dB/m (9–48.8) vs. 14 dB/m (–4.5 to 50); *P*=0.52]. Alterations in BMI and waist circumference were similar between groups. Homeostasis model assessment-estimated insulin resistance (HOMA-IR) [0.68 (0.14–1.69) vs. –0.51 (–1.12 to 0.44); *P*=0.03], triglycerides [34 (–1.5 to 76.8) vs. –10 (–28.5 to 20.5) mg/dL; *P*=0.006], and ALT (43.7±36.7 vs. 28.1±21.5 U/L; *P*=0.04) were significantly improved in the saroglitazar group. Changes in HSI, FAST score, APRI, FIB-4, and liver stiffness were similar between groups. No serious adverse events were observed.

Interpretation and conclusions: In non-obese NAFLD/MASLD patients, the combination of saroglitazar with lifestyle changes over a period of six months improved insulin resistance, triglycerides, and ALT but did not confer additional benefit over lifestyle intervention alone for non-invasive hepatic steatosis or liver fibrosis markers.

Keywords Insulin resistance; MASLD; NAFLD; Non-obese NAFLD; Saroglitazar