

**METFORMIN, WEIGHT  
LOSS AND NAFLD**

Serum alanine aminotransferase (ALT) levels are lower in individuals treated with metformin than placebo, an effect mediated by weight loss, according to the Diabetes Prevention Program Research Group.

Raised ALT levels are common, especially in people with overweight or obesity, and are mostly related to nonalcoholic fatty liver disease (NAFLD). Weight loss is recommended to treat NAFLD as the condition can progress to cirrhosis; however, little research has assessed the efficacy of this strategy. The researchers investigated whether metformin therapy or changes in metabolic measurements had improved serum ALT levels, a biomarker for NAFLD, in the Diabetes Prevention Program trial.

In the metformin arm of this trial, 2,153 participants without markedly elevated ALT levels at baseline were randomly allocated to receive either metformin or placebo for an average of 3.2 years. Participants were  $\geq 25$  years old with a BMI  $> 24$  kg/m<sup>2</sup> and no history of excessive alcohol use.

Serum ALT levels increased in both groups over the first 2 years of the trial. Nonetheless, after adjustment for baseline covariants, serum ALT levels were significantly lower in participants treated with metformin than in those who received placebo. However, after adjustment for changes in weight, and fasting plasma glucose and insulin concentrations, the between-group difference was no longer significant. Analysis of weight loss suggested that this was the dominant factor in reducing ALT levels. However, the researchers admit that it is difficult to distinguish the effects of weight loss from those of changes in insulin and glucose concentration, which also decrease when individuals lose weight.

The researchers conclude that weight loss, either via drug or lifestyle treatment, has a beneficial effect on NAFLD.

*Claire Greenhill*

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