



Fatty Liver Disease Responds to Extra Exercise

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SAN FRANCISCO, July 6 -- Increasing physical activity may improve liver and metabolic manifestations of nonalcoholic fatty liver disease (NAFLD) independent of weight loss, a randomized clinical trial revealed.

Even small changes, such as an extra hour per week of exercise, resulted in significant reductions in ferritin, aspartate and alanine aminotransferases, and gamma glutamyl transpeptidase ($P<0.05$ to $P<0.001$), Jacob George, MBBS, PhD, of the University of Sydney, Australia, and colleagues found.

These effects, as well as the improvements in insulin resistance and other metabolic parameters, remained after adjustment for changes in weight, the researchers reported in the July issue of *Hepatology*.

"This is particularly important as weight loss and weight loss maintenance are often difficult to achieve and not all patients presenting with hepatic steatosis are overweight," they wrote.

Action Points

- Note that the American Heart Association recommends at least 30 minutes of exercise five days per week, or 150 minutes per weeks of physical activity.
- Explain to interested patients that nonalcoholic fatty liver disease reflects an accumulation of fat in the liver that can cause inflammation and scarring.

While lifestyle change has been the primary strategy for treating patients with nonalcoholic fatty liver disease, weight loss through diet has been the main aim of interventions, the researchers said.

So, to determine the impact of an exercise-based strategy, Dr. George's group conducted a randomized, controlled trial looking at different levels of counseling and support for increased physical activity.

The 141 NAFLD patients were randomized to the following groups:

- Low-intensity intervention with counseling sessions at baseline and weeks two and four.
- Moderate-intensity intervention with six counseling sessions over the first three months.
- Moderate-intensity intervention plus additional long-term telephone support in the maintenance period out to 12 months.
- A single consultation at baseline as a control without support, advice, or assistance in making changes to physical activity. After the first three months, the control group was randomized to intervention.

In the counseling sessions, patients got individually tailored advice from exercise scientists encouraging them to increase moderate-intensity physical activity -- primarily walking.

The aim was to achieve at least 150 minutes per week in accord with the American Heart Association recommendation for at least 30 minutes of physical activity, five days per week.

The low- and moderate-intensity interventions both appeared to be effective in increasing physical activity, compared with the nonintervention control, at three months (both $P<0.001$).

The advice and support given to the intervention groups boosted the odds that participants would exercise at least an extra 60 minutes per week 9.2-fold for the low-intensity group and 9.4-fold for the combined moderate-intensity groups, compared with controls (both $P<0.001$).

Likewise, the number who met the physical activity target at three months increased by 35% in the low-intensity group and 25% in the moderate-intensity group (both $P<0.001$ compared with baseline). There was no increase in the control group (-13%, $P>0.05$ versus baseline).

Changes in fitness measured by maximal oxygen uptake (VO_2) corroborated these self-reported changes in physical activity.

The effects of increased exercise were also reflected in metabolic and liver enzyme measures.

Participants who remained sedentary showed no improvement in liver enzymes or any other parameter, despite an average 1.5-kg reduction in weight.

But those who were active with at least 60 minutes of exercise per week, regardless of whether they met the goal, did have significant improvements in every measure of liver enzymes (all $P < 0.05$).

Even after adjustment for change in weight, liver enzyme improvements were greater for every activity level compared with the sedentary group (most $P < 0.05$).

Those who increased their activity level by at least 60 minutes per week had significant improvements in fasting blood glucose, insulin resistance, cholesterol and triglyceride levels, and both fasting and two-hour insulin.

Although the largest effect on liver enzymes was seen in those who either kept their activity at target or had an increase of at least 60 minutes per week, there was no clear dose-response relationship, such that even small changes in physical activity appeared to be as effective as large changes.

"The reason for this is unclear, but we hypothesize that the threshold for change in liver enzymes may be low so that even a slight increase in physical activity is sufficient to improve liver tests," Dr. George's group said, "and additional increases in physical activity may not translate to 'dose-response' reductions in liver enzymes."

However, they noted that their study may not have been powered to detect such a relationship "given the known variability between individuals."

The study results are likely generalizable and more practical to implement in practice than supervised exercise sessions, they concluded.

The study was supported in part by a grant from the National Health and Medical Research Council of Australia and the Robert W. Storr bequest to the University of Sydney.

The researchers reported no conflicts of interest.

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St. George A, et al "Independent effects of physical activity in patients with nonalcoholic fatty liver disease" *Hepatology* 2009; 50: 68-76.

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Dr. Gauranga C.Dhar - Jul 07, 2009

It has well been established that obesity leads to T2DM, but not all obese individuals become diabetics. Research shows that higher the level of liver enzyme, gamma glutamyl transferase (GGT) e.g. $>50\text{u/L}$, higher the chance of development of T2DM, worsening insulin resistance syndrome and increasing cardiometabolic risks (CMR). A considerable portion of obese individuals are found to have non-alcoholic steatohepatitis (NASH). Analysis of the sudden tragic death of Tim Russert, host of "Meet the Press", chief NBC Washington last year probably was due to very high level of GGT; 200u/L ($N < 50\text{u/L}$). Intensive physical exercise reduces all pathologically elevated liver enzymes in patients with NASH may improve metabolic outcomes. In addition to lifestyle modification, are there any drug we can use to treat NASH effectively?

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