



Editorial

Are hepatitis B carriers more vulnerable to exercise-related liver injury? Recent evidence from a 7-day ultramarathon



1. The impact of exercise on liver enzyme tests

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are the most well-known liver enzyme tests used to diagnose hepatocyte injury. Besides, these two enzymes are localized in the liver at high concentrations. AST is also present in the heart, skeletal muscle, kidneys, pancreas, brain, and red blood cells in considerable amounts. However, ALT is present in low concentrations in skeletal muscle and other extrahepatic organs. Therefore, ALT is an indicator of liver damage in most situations, and AST is a less specific marker of liver injury. The presence of these enzymes in the blood is due to changes in membrane permeability as well as cellular disruption, damage, and death. These enzymes are also observed in blood in response to exercise.

Many previous studies have revealed that endurance exercise, especially marathon race, may increase the serum level of ALT, AST, bilirubin, alkaline phosphatase (ALP), lactate dehydrogenase, and creatine kinase, and decrease serum albumin and protein.^{1–6}

During aerobic energy production, aminotransferases can catabolize amino acids, allowing them to enter the citric acid cycle, and thus generating adenosine triphosphate to maintain muscle contraction and substantial physiologic response, such as increased heart and respiratory rates and thermoregulation. It is generally believed that the elevation of ALT and AST levels after exercise originates mainly from muscle, and that only small amounts originate from the liver.^{1–3}

The increase in bilirubin may be caused by foot-strike intravascular hemolysis, intramuscular destruction of red blood cells due to osmotic stress, and membrane lipid peroxidation caused by free radicals released by activated white cells.⁶

ALP is an enzyme that can transport metabolites across cell membranes including lipids for oxidative energy production. Liver and bone diseases are the most common causes of pathological elevation of ALP, followed by intestinal problems. The origin of exercise-related elevation of ALP was believed to arise mainly from osteoblasts in the bone by the stress and stimulation from exercise, although little data regarding the isoenzyme of ALP have been reported in the

literature.⁶ The rise in ALP level may also reflect that liver increases gluconeogenesis and lipid peroxidation activity, and high bone turnover induced by exercise. However, release of ALP from the hepatobiliary system after exercise may play only a minor role in the elevation of serum ALP level.

Albumin is mainly synthesized in the liver, and serum albumin level is regarded as an indicator of liver function representing liver reserve. Decreased serum albumin level after exercise was observed in some studies, which may reflect damage to the anabolic functioning of hepatic cells or the long-term fasting after the marathon. Decreased total protein after exercise was also shown in some reports, which may be merely due to the reduction of serum albumin.⁶

2. Detrimental effect of chronic hepatitis B infection on liver enzyme test in marathon runners

In this issue of the *Journal of the Chinese Medical Association*, Chou et al⁷ intended to investigate the impact of hepatitis B virus (HBV) carrier status on the aforementioned liver enzyme tests during multiday marathon races. This prospective study recruited 10 Taiwanese runners participating in 7-day ultramarathon races, including three HBV carriers. The authors found that there were higher serum ALT, AST, and total bilirubin levels in the HBV carriers compared with the noncarriers, and the time-by-group interaction was also significant for these biomarkers. There were no significant time-by-group effects on the serum ALP, albumin, and total protein levels, but the change over time effect was significant. They concluded that liver functions in HBV carriers are more highly impacted by the 7-day marathon than those in noncarriers. This is the first paper to disclose the potential for liver injury after extended duration marathon running in HBV carriers.

Most of the previous studies suggest that elevated levels of serum transferases and other enzymes after endurance exercise mostly originate from muscle, instead of the liver.^{1–3,6} However, this study highlights the possibility of a hepatic origin of the enzymes, owing to the higher levels of these enzymes in HBV carriers compared with noncarriers.

The same study group has published a relevant paper concerning the influence of a 100-km marathon on HBV

carriers.⁸ In contrast to the present study in this issue, they found no statistical difference in all biomarkers of liver, muscle, and inflammation between HBV carriers and non-carriers. They suggest that HBV carriers do not have higher risks of liver function impairment, muscle breakdown, and inflammatory response compared with noncarriers in the 100-km endurance race.

The different results between these two studies suggest that the duration of exercise may be the key determinant of hepatic damage in HBV carriers.^{7,8} It is unfortunate that there was no direct comparison of data between the 1- and 7-day marathons. The further limitations of the present study are the very limited number of cases and controls, and the absence of data regarding HBV DNA before and after the race. However, the overall number of runners participating in the ultramarathons, especially 7-day races, is extremely low worldwide. However, there were sequential data between HBV carriers and non-carriers during the race in the present study. Therefore, this study is still of value to enhance our understanding of the impact of multiday marathon on the liver function of HBV carriers. However, a prospective study utilizing a larger sample size should be conducted to more reliably reach further conclusions.

3. The mechanism of liver injury by acute exercise

Little is known about how exercise affects the liver during acute exercise. Evidence has shown that arterial inflow supplying the liver is decreased during acute exercise.^{9,10} In fact, the blood flow can be reduced to as low as 20% of its resting value.⁹ It is possible that hypoperfusion of the liver may insult the hepatocytes and thus release liver enzymes into circulation. Furthermore, epithelial integrity and gut wall barrier function might also be compromised with repeated exposure to strenuous physical stress, which is the other explanation regarding release of the associated enzymes into blood. However, evidence provided in the relevant study regarding this point is scant, and the real mechanism is yet to be elucidated.

4. Summary

Exercise, especially participation in a marathon race, may induce elevation of many serum enzymes, representing insult to muscle, liver, or heart. It is generally believed that the increases of these enzymes after exercise are mainly from muscle. In this issue of the *Journal of the Chinese Medical Association*, a study from Taiwan found that there were higher serum ALT, AST, and total bilirubin levels in the HBV carriers compared with the noncarriers in a 7-day ultramarathon race. This result implicates that the liver also contributes to the elevation of these enzymes after exercise, and

that HBV carriers may be more vulnerable to hepatic damage by multiday marathon. Although this finding warrants further large-scale prospective studies to provide additional support, physicians and HBV carriers should be aware of the potential hepatic damage from such acute vigorous exercise.

Conflicts of interest

The author declares that he has no conflicts of interest related to the subject matter or materials discussed in this article.

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Yi-Shin Huang*

Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital and National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC

*Corresponding author. Dr. Yi-Shin Huang, Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.

E-mail address: yshuang@vghtpe.gov.tw.