

A Study of Transaminases in Heroin Addicts

Rino A. Gani, Agus S. Waspodo, Unggul Budihusodo, Irsan Hasan, H.M. Sjaifoellah Noer

Division of Hepatology, Department of Internal Medicine
Medical Faculty, University of Indonesia

ABSTRACT

A recent increase in the number of drug users particularly of heroin has been noted in the community. A cross-sectional study on the level of transaminases as a representation of liver damage in drug users was done in privated hospital in Jakarta. Exclusion criteria were fever, serious illness or the multiple use of addictive drugs based on a urinary test. The hepatitis B surface antigen (HBsAg) was examined using reverse passive hemagglutination assay (RPHA) and the antibody of hepatitis C virus core-protein (anti-HCV) with dipstick anti-HCV. AST and ALT levels were determined using an automatic chemical analyzer. Of 132 patients who fulfill the criteria, 83.5 % were injection drug users (IDU). Means AST and ALT were significantly higher in IDU. Anti-HCV positive patients with increased AST and ALT were significantly higher compared to anti-HCV negative. The increase of transaminase was also consistent in injection drug users although no viral marker could be detected. In conclusion, the examination of transaminases in drug users especially IDU is important besides tests for hepatitis viral markers because there is often an increase with or without viral infection and this can be associated with hepatocellular damage.

Key words: Transaminase, heroin addicts, hepatitis.

INTRODUCTION

Recently, large cities in Indonesia have been faced with an increasing number of drug users, especially among teenagers. Jakarta, as the capital of Indonesia and one of the metropolitan cities in Asia may have the biggest problem of drug abuse in Indonesia. This city is no longer just a transit place for drugs traffic but has become a major target. There is no official data regarding this in Indonesia but anecdotal reports clearly show the very fast increment of drug use. It is estimated that the number of drug users now in Indonesia is about 2 million people.

Drug use causes both social and medical problems. The medical problem is not just merely the addiction but also several diseases caused by microorganisms which are introduced because of their high-risk behavior. The highest risk group is the heroin addicts who often use non-aseptic, shared syringes and needles. Among them the transmission of virus such as hepatitis C virus (HCV), hepatitis B virus (HBV) and Human Immunodeficient

Virus (HIV) is common.

In the past, there has been no published report regarding the impact of viral hepatitis in drug users because of the insignificant number of them in the community or hospitals. A relatively large population study of viral hepatitis in Jakarta 7 years ago have found only a very small number of drug users in community.¹ The recent rise in the number of drug users in Indonesia may change the proportion of viral hepatitis patients and its influence in liver diseases in Indonesia.

We study the transaminases as an indication of liver damage in heroin drug users addicts in connection with the method of drugs usage (injection and non-injection) and viral hepatitis infection.

MATERIAL AND METHOD

This study was done from March 1999 to July 1999 in a private hospital located in the center of Jakarta (Mitra Menteng Abadi Hospital). Data was collected consecutively from patients who were admitted for rehabilitation

or drug related complications with a positive urine test for heroin. Patients were excluded from the study if they had fever, serious illness, anti-HIV positive or on the multiple use of addictive drugs based on anamnesis and urinary test for multiple drugs.

The hepatitis B surface antigen (HBsAg) was examined using reverse passive hemagglutination assay (RPHA) and the antibody of hepatitis C virus core-protein (anti-HCV) with dipstick anti-HCV, anti-HIV with dipstick anti-HIV from Laboratorium Hepatika, Mataram, Indonesia. The dipstick method for anti-HCV detection has been shown to have equal sensitivity to commonly used second-generation enzyme-linked immunosorbent assay.² AST and ALT level were determined using automatic chemical analyzer with cut-off value of 24 U/mL for AST and 27 U/mL for ALT.

Data was compiled and analyzed using Statistical Product and Service Solutions (SPSS) 7.5 for Windows (University of California Davis). Chi-square or Fisher exact test was applied to compare the value between the two groups. A significant level was assumed if $p < 0.05$.

RESULTS

There were 162 patients, of these 133 (82 %) fulfill the criteria for study as described above. The patients characteristics are shown in table 1.

Mean ALT and AST level in the injection group was higher than in the non-injection heroin addicts ($35.9 \text{ U/mL} \pm 45.5$ Vs $21.3 \pm 35.4 \text{ U/mL}$ and $52.6 \pm 68.2 \text{ U/mL}$ Vs $33.8 \pm 62.4 \text{ U/mL}$, respectively). The ALT level was greater than the AST level in both groups showing that the hepatocellular damage were more likely to be in the acute phase. As showed in table 2, the numbers of patients with increased ALT and AST were significantly higher in the injection group compared to the non-injection heroin addicts. Table 3 shows the AST and ALT value according to the virological status of the patients.

A significant difference of increased AST and ALT occurred in Anti-HCV positive compared to negative patients. But in the HBsAg group, the number of patients with increased AST and ALT was not different between the HBsAg negatives and positives.

The increase of transaminase was also consistent in injection drug user albeit there were no viral marker

Table 1. All heroin addicts characteristics.

| n = 133 patients | n | % |
|------------------------------------|-----------------|----------|
| Sex : male | 118 | 88,7 |
| female | 15 | 11,3 |
| Mean age (year) | 21.1 ± 3.7 | |
| Mean duration of drug use (months) | 27.9 ± 19 | |
| Method of drug use : injection | 111 | 83,5 |
| non-injection | 22 | 16,5 |
| Mean AST (U/L) \pm SD | 33.5 ± 44.2 | |
| Mean ALT (U/L) \pm SD | 49.5 ± 67.5 | |
| HBsAg positive (%) | 6 | 4,5 |
| Anti-HCV positive (%) | 80 | 60.2 |
| HBsAg and Anti-HCV positive (%) | 16 | 12 |

Table 2. Proportion of increase AST and ALT in injection and non-injection heroin addicts.

| Method of heroin usage | AST | | ALT | |
|------------------------|-----------|-----------|-----------|-----------|
| | increased | normal | increased | normal |
| Injection (%) | 52 (39.1) | 59 (44.4) | 62 (46.6) | 49 (36.8) |
| Non-injection (%) | 3 (2.3) | 19 (14.3) | 4 (3.0) | 18 (13.5) |
| p-value* | 0.004 | | 0.001 | |

* χ^2 -test.

Table 3. AST and ALT value according to viral marker in heroin addicts (n = 133).

| | | Anti-HCV | | p* | HBsAg | | p* |
|------------|--------------|-----------|-----------|-------|-----------|----------|----|
| | | negative | positive | | negative | positive | |
| AST | normal (%) | 28 (23.9) | 42 (35.9) | 0.017 | 66 (56.4) | 4 (3.4) | NS |
| | increase (%) | 9 (7.7) | 46 (32.5) | | 45 (38.5) | 2 (1.7) | |
| ALT | normal (%) | 26 (22.2) | 33 (28.2) | 0.004 | 55 (47.0) | 4 (3.4) | NS |
| | increase (%) | 11 (9.4) | 47 (40.2) | | 56 (47.9) | 2 (1.7) | |

* X²-test

Table 4. ALT and AST value in heroin addicts with HBsAg and Anti-HCV negative (n = 31)

| | AST | | ALT | |
|-------------------|----------|-----------|----------|-----------|
| | Increase | Normal | Increase | Normal |
| Injection (%) | 7 (22.6) | 12 (38.7) | 8 (36.3) | 11 (35.5) |
| Non-injection (%) | 0 | 12 (38.7) | 1 (3.2) | 11 (35.5) |
| p* | 0.017 | | NS | |

X²-test.

which could be detected. Table 4. shows the AST and ALT level in patients with HBsAg negative and Anti-HCV negative.

The number of patients with an increased level of AST was significantly more than normal. Therefore, it is possible that hepatocellular damage or dysfunction also occurred in patients without hepatitis C or B infection and other causes must be considered.

DISCUSSION

Transaminase is enzyme test that is usually performed to asses the hepatocellular damage and AST and ALT are the most frequently used tests for this reason. A rise in these enzymes is implicated by the increase in cellular damage or dysfunction in the liver.³

Most of the drug users that we studied used heroin by injection. They mixed the powder with non-sterilized liquid. Heroin packages that are sold illegally in the street are usually mixed with other substances that are not completely known. Moreover, they usually share syringes and needles with other drug users which are kept in non-sterilized conditions which allow transmission of micro-organisms. These can all be the reasons for the increased transaminases, particularly in injection drug users as shown in table 2.

The mean duration of heroin usage is about two years, so they have been exposed to the damaging substances for quiet some time. These patients will need a long term

follow up to ascertain the influence of this matter in the future because of the chance of developing chronic liver diseases.

Infection with hepatitis C but not hepatitis B virus is strongly associated with hepatocellular damage in our series. ALT levels were increased in 57.3 % (55/96 patients) with anti-HCV positive and more patients have an increase of ALT than of AST which is more likely to indicate acute infection.³ More than half of the patients with hepatitis C virus infection have increased ALT. Our results were in-line with other studies.⁴ This may bring problems in the future because in this kind of patient liver disease tends to develop in to more severe liver damage.⁵ Further-more, the normal ALT level in patients with anti-HCV positive must have a thorough prospective investigation because the ALT level in hepatitis C virus infection can fluctuate and this study revealed that some of them are not completely free from hepatocellular damage.^{5,6}

In the co-infection of hepatitis B and C viruses, the transaminase also increased, that is suggestive of the more explicit impact of hepatitis C virus infection because in the single hepatitis B virus infection, transaminases were normal. The expression of hepatitis B virus is often masked with hepatitis C virus if the patient is co-infected but the risk of developing hepatocellular cancer is much greater compared to a single infection with either virus.^{7,8}

The number of hepatitis B patients who were not co-infected with hepatitis C virus is about the same to the prevalence of hepatitis B infection in general population¹ suggested that they have the same route of transmission. In this kind of individual, the hepatitis B infection usually occurred perinatally, therefore the transaminases were not increased because of immune tolerance. Other studies of hepatitis B in drug users also made the same conclusion.⁹ Worth mentioning that in adults, 80 - 90 % hepatitis B virus infection resulted in complete viral clearance where HBsAg can not be detected anymore.⁷ In this study we used HBsAg as a marker only for persistent infection of hepatitis B virus.

Viral infections were not the only cause of hepatocellular damage in drug users. The number of injection drug users with raised transaminase particularly AST was significantly higher than the normal one although no viral marker had been detected. It is possible that they have a seronegative viral infection or some other hepatotropic viral infection which was not detected in this study but another possibility, such as hepatotoxicity from an injected substance is worth considering. The reason as to why the AST and not the ALT is significantly increased in IDU without HBsAg or Anti-HCV is not clear but this pattern is somewhat different to the pattern of increased transaminases in association with hepatitis B or C virus infection, suggesting that a different mechanism is involved. This finding may be the result of chronic hepatocellular damage since AST was shown to be increased more in chronic liver diseases and these patients have already used heroin by injection for more than 6 months but the possibility of other organ damage must be contemplated since AST is also found in other organs such as heart.³

In conclusion, the examination of transaminases in drug users, especially IDU is important because it is often increase with or without viral infection and it can be

a reflection of hepatocellular damage. Since the use of drugs for detoxification and to block endorphin receptors can also have some degree of hepatotoxicity, the possibility of increased risk of drug induced hepatitis must be considered. These drugs must be used judiciously in IDU.

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REFERENCES

1. Akbar N, Basuki B, Mulyanto, Garabrant DH, Sulaiman A, Noer MS. Ethnicity, socioeconomic status, transfusions and risk of hepatitis B and hepatitis C infection. *J Gastroenterol Hepatol* 1997; 12:752-7.
2. Mulyanto, Suwignyo S, Tsaury S et al. An easy dipstick assay for anti-core antibodies to screen blood donors for hepatitis C virus viremia. *Vox Sang* 1996;70:229-31.
3. Sherlock S, Dooley J. Assessment of liver function. In: *Disease of the liver and biliary system*. 10th ed, Blackwell Science 1997: 17-32.
4. Ingelsby TV, Rai R, Astemborski J, et al. A prospective, community-based evaluation of liver enzyme in individuals with hepatitis C after drug use. *Hepatology* 1999;29(2):590-6.
5. Marcellin P. Hepatitis C: the clinical spectrum of disease. *J hepatol* 1999;31: (Suppl.1):9-16.
6. Pradat P, Poynard T, Alberti A, et al. Predictive value of ALT levels on histological findings in chronic hepatitis C: A European Collaborative Study. *J Hepatol* 2001;34: (Suppl. 1):5.
7. Chan HLY, Lok ASF. Hepatitis B in adults. A clinical perspective. *Clin Liver Dis* 1999;3(2):291-307.
8. Bukh J, Miller RH, Kew MC, et al. Hepatitis C virus RNA in Southern African blacks with hepatocellular carcinoma. *Proc Natl Acad Sci USA* 1993;90:1848-51.
9. Maayan S, Shufman EN, Engelhard D, Shouval D. Exposure to hepatitis B and C and to HTLV-1 and 2 among Israeli drug abusers in Jerusalem. *Addiction* 1994;89(7):869-74.