

Plasma level of nitric oxide and the expression of inducible nitric oxide synthase in human hepatocellular carcinoma

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Received: May 6, 2000
Revised: June 10, 2000
Accepted: July 10, 2000
Published online: September 15, 2000

Abstract

AIM: To study the relationship between nitric oxide (NO), nitric oxide synthase (NOS) and human hepatocellular carcinoma (HCC).

METHODS: Plasma $\text{NO}_2^-/\text{NO}_3^-$ was measured by Griess reaction in 122 patients with chronic hepatitis (CH) and compensated liver cirrhosis (LC), among which 62 patients were complicated with HCC (CH = 28, LC = 34), and the rest 60 patients were not (CH = 29, LC = 31). Thirty healthy persons served as normal controls (NC). There were no prominent differences among the groups in sex, age and the ratio of CH to LC. The expression of inducible nitric oxide synthase (iNOS) in HCC ($n = 40$), CH ($n = 30$) and LC ($n = 30$) samples obtained from liver biopsy or operation was compared with that in normal liver tissues by using immunohistochemistry. Ten normal liver tissue samples obtained from liver operation served as normal controls.

The samples were fixed in formalin and embedded in paraffin. Anti-iNOS antibody (Santacruz company) was served as antibody- I in immunohistochemical assay of iNOS in tissue.

RESULTS: Plasma $\text{NO}_2^-/\text{NO}_3^-$ level in normal was $11.5 \pm 4.2 \mu\text{mol/L}$. The plasma level of $\text{NO}_2^-/\text{NO}_3^-$ in CH ($58.6 \pm 17.4 \mu\text{mol/L}$) and LC ($38.7 \pm 10.6 \mu\text{mol/L}$) accompanied with HCC was notably higher than in those patients without HCC (CH: $24.8 \pm 9.4 \mu\text{mol/L}$; LC: $22.3 \pm 8.7 \mu\text{mol/L}$, $t = 2.901, 2.756, P < 0.01$). Plasma $\text{NO}_2^-/\text{NO}_3^-$ level in HCC accompanied with CH was significantly higher than in those accompanied with LC ($t = 2.216, P < 0.05$). Positive rate of iNOS in HCC, CH and LC was 95%, 93% and 57% respectively. iNOS was not expressed in normal liver tissues. The expression level of iNOS in HCC ($\chi^2 = 17.4, P < 0.001$) and CH ($\chi^2 = 11.64, P < 0.025$) was much higher than in LC.

CONCLUSION: Plasma $\text{NO}_2^-/\text{NO}_3^-$ level significantly increased in patients with HCC and the immunohistochemical staining of iNOS was positive. This suggests that the liver secretes NO in the higher level may participate in the carcinogenesis and progression of HCC.

Key words: Liver neoplasms; Nitric oxide/blood; Nitric oxide synthase; Hepatitis; Liver cirrhosis; Immunohistochemistry; Hepatoma

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Shao RX, Wang JB, Guo JH. Plasma level of nitric oxide and the expression of inducible nitric oxide synthase in human hepatocellular carcinoma. *World J Gastroenterol* 2000; 6(Suppl3): 102 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v6/iSuppl3/102.htm> DOI: <http://dx.doi.org/10.3748/wjg.v6.iSuppl3.102>

E- Editor: Zhang FF



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