Clinical significance of Golgi protein 73 in hepatocellular carcinoma patients

Thesis Presented BY

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Summary and conclusion

Hepatocellular carcinoma (HCC) is ranked the fifth most common cancer and the third most common cause of cancer-related death worldwide. HCC occurs two to four times more often among men than women and within an established background of chronic liver disease.

The present study aims to estimate serum level of Golgi protein 73 and Interleukin-17 in HCC patients to assess them as markers for HCC diagnosis.

This study was carried out on:

1) Hepatocellular carcinoma patients:
   - This group consisted of 50 HCC patients selected from the Oncology Center, Faculty of Medicine, Mansoura University, Mansoura.
   - They included 40 males and 10 females with ages ranged between 38-76 years with a mean ± SE of 58.84 ± 1.15.

2) Patients with hepatic cirrhosis:
   - This group consisted of 30 cirrhotic patients selected from the Specialized Medical Hospital, Faculty of Medicine, Mansoura University, Mansoura, Egypt.
   - They included 17 males and 13 females, with ages ranged between 32-81 years with a mean ± SE of 57.8±1.85.

3) Control group:
   - The control group consisted of 8 apparently healthy subjects with ages ranged between 45 – 65 years with a mean ± SE of 53.75 ± 2.45
   - They included 3 males and 5 females with no apparent evidence of medical disorder or active disease.

Both cirrhotic and HCC patients were classified according to Pugh's modification of Child classification into:

- Class A: 38 HCC patients and 10 cirrhotic patients.
- Class B: 9 HCC patients and 8 cirrhotic patients.
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- Class C: 3 HCC patients and 12 cirrhotic patients.

Moreover, HCC patients were classified according to Barcelona- Clinic Liver Cancer Group diagnostic and treatment strategy (BCLC) into:

- Stage A, 10 HCC patients.
- Stage B, 19 HCC patients.
- Stage C, 17 HCC patients.
- Stage D, 4 HCC patients.

Serum was used for estimation of liver function tests (ALT & AST activities, total bilirubin, and albumin levels). Hb concentration was determined by colorimetric method. White blood cells, red blood corpuscles and platelets were counted by hemocytometer apparatus. Furthermore, Serum levels of \( \alpha \)-fetoprotein (AFP), Golgi protein 73 (GP73) and Interleukin-17 (IL-17) were measured using commercially available human enzyme linked immuno-sorbant assay (ELISA) kits.

Serum AFP increased significantly in HCC group as compared to both cirrhotic and control group. Serum AFP at a cut-off value of 200 (ng/ml) in HCC patients showed a sensitivity of 50%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 60%.

Serum Golgi protein 73 level increased significantly in HCC and cirrhotic patients as compared to control group, but HCC group showed non-significant difference as compared to cirrhotic group.

Serum GP73 at a cut-off 16 ng/ml in HCC patients showed sensitivity, specificity, positive predictive value, negative predictive value, 56%, 42.1%, 56%, and 42.1%, respectively. The combined determination of AFP and GP73 had a sensitivity of 76% in determination of HCC patients.

Serum interleukin-17 level increased significantly in HCC patients when compared to both cirrhotic and control groups. On the other hand, there was non-significant increase in serum IL-17 in cirrhotic patients when compared to control group.

Serum IL-17 was significantly correlated with performance status, ascites, distant metastasis and portal vein invasion. Also, it was significantly correlated with child score
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and tumor stage as defined by BCLC. Serum IL-17 was negatively correlated with the overall survival rate, at a cut-off < 3 pg/ml the overall survival rate was 24 month, but at a cut-off ≥ 3 pg/ml, the overall survival rate was 10 months.

Serum IL-17 at a cut-off 3 pg/ml in HCC patients showed sensitivity, specificity, positive predictive value, negative predictive value of 54%, 60.5%, 64.2%, and 50%, respectively. The combined determination of AFP and IL-17 had a sensitivity of 74% in diagnosis of HCC patients.

From these results we can conclude that:

- Serum Alpha-fetoprotein, the most widely used tumor marker, had high specificity but low sensitivity.
- Serum Golgi protein 73, unlike many previous studies, is not a valuable diagnostic marker for HCC due to its low sensitivity and low specificity. It can only be used as marker of liver disease.
- Serum IL-17 can be used as a new hepatocellular carcinoma marker. It has higher sensitivity than AFP. Serum IL-17 in the present study was significantly related to HCC stages and other poor prognostic criteria like portal vein invasion, presence of distant metastasis and low survival rate. So it can be used as a potential prognostic marker.
- More characterization of IL-17 effect on HCC metastasis and invasion may contribute to the identification of new diagnostic marker and therapeutic targets.
- Combined use of AFP and IL-17 is of value to increase the sensitivity for HCC diagnosis and also for prognosis.
- Further studies were needed for evaluation of the diagnostic and prognostic values of IL-17 as a biomarker for HCC.