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Diabetes mellitus impairs the response of intra-arterial chemotherapy in hepatocellular carcinoma

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Background: Diabetes mellitus has been associated with poorer outcome in patients with hepatocellular carcinoma, but the influence of diabetic conditions on chemotherapy remains uncertain. Intra-arterial chemotherapy is one of the treatment modalities for advanced hepatocellular carcinoma. The study compares the response of intra-arterial chemotherapy on diabetic or non-diabetic patients with advanced hepatocellular carcinoma.
Material and Methods: Between August 2007 and May 2008, 52 patients with unresectable advanced hepatocellular carcinoma underwent intra-arterial chemotherapy with cisplatin and fluorouracil. Tumor response was assessed by computed tomography or magnetic resonance imaging. *In vitro*, hepatocellular carcinoma cell line Hep G2 was evaluated for cytotoixc effect of cisplatin and fluorouracil in different concentrations of insulin and glucose mimicking diabetic conditions.
Results: Among the 52 patients, 14 were diabetic while 38 were non-diabetic. The partial response rate was similar in the two groups (14% in diabetics and 18% in non-diabetics). Non-diabetic patients had a lower rate of progressive disease (16% vs 43%, $p = 0.039$). The median time to disease progression was found to be significantly longer in non-diabetics compared with the diabetic counterpart (a median of 206 days vs 88 days, $p = 0.02$). The proliferation of hepatocellular carcinoma cell line Hep G2 cells was promoted in the increasing concentration of insulin from normal physiological concentration, 0.0005 mg/L to hyperinsulinemia status, 5 mg/L. In the presence of chemotherapy agents, cisplatin and fluorouracil, Hep G2 cells showed less cytotoxic effect while treated with higher concentrations of insulin. On the other hand, the proliferation of Hep G2 cells was not influenced significantly by different concentrations of glucose even in the conditions with cisplatin or fluorouracil.
Conclusions: Our study showed that intra-hepatic chemotherapy for unresectable hepatocellular carcinoma was less effective in diabetic patients than non-diabetic counterpart in terms of progression free rate and time to disease progression survival. Insulin, rather than glucose, stimulated hepatocellular carcinoma cells, Hep G2, to proliferate rapidly and enhanced the resistance to chemotherapeutic agents, cisplatin and fluorouracil. These results emphasize the important role of diabetes mellitus in chemotherapy treatment of advanced hepatocellular carcinoma.

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Hepatocellular carcinoma presenting with lung metastasis: clinical characteristics and prognostic factors

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Background: The efficacy of systemic chemotherapy for hepatocellular carcinoma (HCC) has been limited, but sorafenib has changed the strategy treating for metastatic HCC. The lung is one of the most common metastatic sites for HCC. Therefore, we focused on clinical features and prognostic factors of HCC patients (pts) with lung metastasis in this study.
Methods: Between January 2000 and April 2008, 1,117 HCC pts were admitted into our division. During this period, extrahepatic metastasis was detected in 278 pts, and the initial metastatic site was lung in 130 pts. The relationships between the characteristics of these pts at the time of lung metastasis detection and prognosis were examined.
Results: There were 106 males and 24 females. Median age was 64 years. The Child-Pugh classification was A in 92 pts, B in 37 pts. HCV Ab was positive in 57 pts, HBs Ag was positive in 46 pts, and both were negative in 27 pts. The median survival time of all pts was 286 days. Univariate analysis revealed 15 of the 21 variables evaluated to be significantly associated with survival time: sex, number of lung metastasis, presence of intrahepatic HCC, maximum size of intrahepatic HCC, presence of tumor thrombus, AFP, PIVKA II, albumin, prothrombin time, ALP, hemoglobin, presence of ascites, Child-Pugh classification, previous systemic chemotherapy and previous history of hepatic resection. Multivariate analysis using the Cox proportional hazards model demonstrated a lower number (<5) of lung metastases ($p < 0.0001$), the systemic chemotherapy after lung metastasis ($p = 0.0005$), the absence of ascites ($p = 0.0008$), the absence of intrahepatic HCC ($p = 0.0050$), AFP (<2000) ($p = 0.0069$), and absence of tumor thrombus ($p = 0.0295$) to be independent favorable prognostic factors.
Conclusions: These results may provide useful reference data for determining treatment strategies and planning further clinical trials involving HCC patients with lung metastasis.

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Hepatocellular carcinoma: a retrospective analysis of 276 cases

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Background & Objective: This study aimed at documenting the spectrum of clinicopathological variations in hepatocellular carcinoma (HCC).
Design: It was a retrospective study.
Place and Duration of Study: This study was conducted at the Institute of Nuclear Medicine and Oncology (INMOL) Hospital, Lahore, Pakistan from March 1997 to July 2008.
Materials & Methods: The profiles of 276 patients with a biopsy proven hepatocellular carcinoma were analyzed in this period. The data collected was age, sex, clinical presentation and laboratory investigations including liver function tests, alpha fetoprotein and hepatitis profile.
Results: Weight loss, jaundice and right upper quadrant abdominal pain were the main presenting symptoms. Out of 276 patients, alpha fetoprotein values were raised in 201 (72.83%) patients. 165 (59.78%) patients were found to have or have had HBV (hepatitis B virus) and 211 (76.45%) patients were anti-HCV (hepatitis C virus) positive. 193 (69.93%) patients were cirrhotic. History of alcohol abuse was found in 9 patients.
Conclusion: The common association of HCC with cirrhosis and hepatitis B and C suggests that vaccination against HBV on nationwide basis can decrease prevalence of this malignancy. There is a need to generate public awareness regarding the transmission of these viruses. Early diagnosis and intervention is also important to the successful management of HCC.

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Investigation of the efficacy on transcatheter arterial chemoembolization combined with or without Chinese herbal therapy for hepatocellular carcinoma: meta-analysis

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Background: In recent years, there has been a great interest in complementary and alternative treatment for cancer. Traditional Chinese medicine (TCM) is sometimes used in conjunction with transcatheter arterial chemoembolization (TACE) for the treatment of HCC in Asian countries. The main objective of this study is to systemically review the efficacy of TCM therapy in hepatocellular carcinoma (HCC) patients receiving TACE.
Materials and Methods: Meta-analysis was performed for randomized controlled trials (RCTs) comparing TCM administration *versus* no TCM treatment given to HCC patients receiving TACE. Overall survival and tumor response were the primary end points. English and non-English publications in ten electronic databases (CNKI, VIP, CDSR, EMBASE, EMDP, MEDLINE, CAB Abstracts, EBM Reviews, AMED, and CINAHL) were extensively searched from 1910 to February 2009. Two review authors assessed trial quality and extracted data independently. The method used for this systematic review followed the Quality of Reporting of Meta-analyses guidelines.
Results: Thirty RCTs involving 2428 HCC patients treated with TACE were included. Treatment with TCM was associated with a significant rise in the number of patients with survival >1-year (odds ratio (OR) 1.92, 95% confidence interval 1.43 to 2.57), survival >2-year (OR 3.55, 2.36 to 5.36), and survival >3-year (OR 5.12, 2.76 to 9.52), a significant rise in the number of patients reported complete or partial response (OR 1.87, 1.53 to 2.28) and non-deterioration performance status (OR 3.78, 2.58 to 5.55), a significant increase in $CD3^+$ T cell level (weighted mean difference (WMD) 13.80, 95% confidence interval 11.86 to 15.73), $CD4^+$ T cell level (WMD 4.54, 2.19 to 6.89), and natural killer cell level (WMD 7.77, 4.30 to 11.24), a significant lower blood alpha-fetoprotein concentration (WMD 131.27, 86.58 to 175.96), a significant increase in white blood cell count (WMD −1.85, −2.88 to −0.82), a significant lower risk in patients with grade 2−4 nausea and vomiting (OR 0.24, 0.10 to 0.57), and a significant rise in patients with increased or stable body weight (OR 3.75, 1.48 to 9.49).
Conclusions: The evidence from this review supports the use of TCM to enhance the efficacy of TACE in HCC patients. Funnel plots have demonstrated no publication bias for the meta-analyses of primary