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Local radiative treatment of hepatocellular cancer with phosphorus-32 glass microspheres to enhance the efficacy of hepatic artery chemoembolism and possibly related with MDR expressed P-glycoprotein

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Abstract

AIM: To investigate the local effect of phosphorus-32 glass microspheres (32P-GMS) on hepatocellular cancer and its relation with chemoembolism.

METHODS: (1) Thirty-two BALB/c nu/nu nude mice were divided randomly into four groups, control group and 3 treatment groups. Every mouse was implanted with human liver cancer cell line subset (H-CS). 32P-GMS amalgamated in iodine oil was injected directly into the tumor mass. After 2 wk, all animals but those in the control group, were injected with 32P-GMS in the dosage of 880 cGY, 1760 cGY and 3520 cGY for mouce groups Ⅰ, Ⅱ and Ⅲ respectively. The histological reactions of tumor mass were observed;multidrug resistance (MDR) expressed p-glycoprotein was detected by flow cytometry. (2) Forty three patients with hepatocellular carcinoma based on the evidence from B sonography or CT and serum AFP > 400 ng/mL or cytological and histological evidences in some cases with the negative AFP were divided randomly into two groups, group Ⅰ treated with 32P-GMS (absorbed dose of 50-100 Gy) alone, group Ⅱ treated with 32P-GMS and chemotherapeutics (half-dosage, doxorubicin 20 mg/m^2, cisplatin 30 mg/m^2). 32P-GMS was injected through intra hepatic artery in these cases with single massive type and multi-nodular type. Every patient was repeatedly treated with this method for 2-3 times. For evaluating the therapeutic results. The modified WHO criteria for tumor therapy standard is the.

RESULTS: (1) Animal bearing tumors showed that the mass decreased markedly and the inhibitive rates attained 66.53%, 83.06% and 91.53% in the absorbed doses ranged form 880 Gy, 1760 Gy and 3520 Gy respectively ($P < 0.05$, ANOVA). Flow cytometry detected MDR expressed p-glycoprotein decreased from 68.2 ± 4.6 in control to 43.6 ± 3.4, 35.3 ± 4.3 and 33.2 ± 3.8 ($P < 0.05$, compared with control, t-test) in the cells from the tumors. (2) The foci in group Ⅰ revealed decreased in size dramatically with effective rate of 71.43%, compared with 86.36% in the group Ⅱ ($P<0.05$, Chi-squaur test). The median survival period of the patients were 532 and 564 d in group Ⅰ and Ⅱ respectively (Kaplan-Meire method).

CONCLUSION: The enhanced effectiveness of the local treatment of 32P-GMS conjugated with chemotherapeutics may be related to the local action on the MDR expressed p-glycoprotein.

Key words: Liver neoplasms/radiotherapy; Liver neoplasms/drug therapy; Phosphorus-32 glass microspheres; Chemoembolization, therapeutic; P-glycoprotein; Multidrug resistance

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