



Altered Metabolism of Drug 4-Methylumbelliferone (4-MU) in Patients with Liver Cancer

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SUMMARY. 4-methylumbelliferone (4-MU) is a typical inhibitor of hyaluronan synthesis, and exerts important utilization in the treatment of various cancers, especially for liver cancers. The present study aims to determine the metabolism alteration of 4-MU in patients with liver cancers, and also tried to find a reliable biochemical biomarker to monitor the metabolism alteration of 4-MU. Thirty patients with liver cancers were enrolled in Cancer Hospital of Shantou University Medical College. Ten mL of peripheral blood was collected, and serum was prepared using two consecutive centrifugation steps. Serum alanine and aspartate aminotransferase (ALT and AST, respectively) activities evaluated. The glucuronidation activity of 4-MU was determined using *in vitro* glucuronidation incubation system. Among the patients with liver cancers, 17 patients had abnormal ALT activities (the threshold of ALT = 50 U/L), and the percentage was calculated to be 56.7%. For AST activity, 20 patients showed abnormal value (the threshold of AST=50 U/L). Good correlation was found between the activity of ALT and the activity of 4-MU glucuronidation ($R^2=0.9$). However, the activity of AST has poor correlation with the glucuronidation activity of 4-MU ($R^2=0.19$). In conclusion, the metabolism alteration of 4-MU was found in patients with liver cancer, and the activity of ALT was demonstrated to be the reliable biomarker to monitor the metabolism alteration of 4-MU in patients with liver cancer.

RESUMEN. 4-metilumbeliferona (4-MU) es un inhibidor típico de la síntesis de hialuronano y es utilizada en el tratamiento de varios tipos de cáncer, especialmente cánceres de hígado. El presente estudio tiene como objetivo determinar la alteración en el metabolismo de 4-MU en pacientes con cánceres de hígado y encontrar un biomarcador bioquímico fiable para controlar la alteración en el metabolismo de 4-MU. Treinta pacientes con cánceres de hígado se inscribieron en el Hospital del Cáncer del Shantou University Medical College. Se recogieron 10 mL de sangre periférica, se preparó el suero utilizando dos pasos de centrifugación consecutivos y se evaluó la actividad de la alanine-y aspartate-aminotransferasa (ALT y AST, respectivamente). La actividad de glucuronidación de 4-MU se determinó utilizando en el sistema de incubación *in vitro*. Entre los pacientes con cánceres de hígado, 17 tenían actividades anormales de ALT (el umbral de la ALT = 50 U/L) y el porcentaje fue 56,7%. Para la actividad AST, 20 pacientes mostraron valor anormal (el umbral de AST = 50 U/L). Se encontró una buena correlación entre la actividad de ALT y la actividad de 4-MU glucuronidación ($R^2 = 0,9$). Sin embargo, la actividad de AST tiene poca correlación con la actividad de glucuronidación de 4-MU ($R^2 = 0,19$). En conclusión, se determinó que en pacientes con cáncer de hígado hay alteración en el metabolismo de 4-MU y que la actividad de ALT demuestra ser un biomarcador fiable para controlar la alteración en el metabolismo de 4-MU en pacientes con cáncer de hígado.

KEY WORDS: alanine aminotransferase (ALT), aspartate aminotransferase (AST), liver cancer, 4-methylumbelliferone.

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