

Study on hepatobiliary disposition of etoposide in an isolated perfused rat liver model (IPRL)

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Background and Aims: Etoposide is an anticancer agent which is used in different malignancies such as lung cancer, testis cancer and leukemia. Etoposide is removed from body by renal and hepatic elimination, two major pathways for drug clearance, in human and animal.

Methods: An Isolated perfused rat liver model was used to investigate the hepatobiliary disposition of etoposide. Portal vein, bile duct and superior vena cava were cannulated in 6 male rat weigh between 250 and 300 gram. The perfusions were conducted using 200 ml freshly prepared buffer Krebs-Henseleit containing glucose and etoposide in concentration of 10mcg/ml (2mg etoposide in 200 ml buffer perfusion). Samples were collected up to 180 min in 10min intervals for perfusate samples and 60 min intervals for bile samples. Determination of etoposide in perfusate and bile samples and homogenized liver was performed by HPLC method using UV detector (λ 285 nm). The separation was performed on RP-18 column under isocratic elution. The mobile phase was a mixture of KH₂PO₄:Acetonitrile:Methanol(55:25:20) and pumped by a flow rate of 1 ml/min.

Results: Concentration of etoposide decreased about 60% in perfusate samples in a log linear pattern. Less than 30% of total parent drug has been recovered in bile samples as cumulative amount of drug and about 5% of administered dose of etoposide was detected in homogenized liver.

Conclusions: This data suggested that hepatobiliary disposition of etoposide plays an important role in drug clearance and could be a dominant site for drug interactions of etoposide with other chemotherapy agents.

Keywords: Etoposide; Hepatobiliary disposition; IPRL