

PHARMACOKINETIC EVALUATION OF LIPOSOMAL AMPHOTERICIN B IN ADULT PRIMARY AND SECONDARY LUNG TUMOR PATIENTS

*Lequaglie C, Brega Massone PP, Conti B, Giudice G, Cataldo I, Scaglione F°, Fraschini F°, Demartini G°,
Oncologic Thoracic Surgery, Istituto Nazionale Tumori of Milan, °Department of Pharmacology University of Milan, Italy

The last years showed new formulations of Amphotericin B (AmB) more simple to use than the old AmB. The first limitation to treatment with AmB is the toxicity. Liposomal-AmB (L-AmB), like other formulations, made possible good results minimizing adverse reactions. The aim of this study was to verify the kinetic curves of L-AmB in the serum and in the lung tissue of lung tumor resected patients. To estimate the long-term concentration and define the L-AmB long-acting in lung tissue; to estimate the plasmatic concentration progressive reduction and define a possible unadverse collateral effect for the decrease in serum. Between March to June 2001 we enrolled 18 adult (>18 ys) patients with primary or secondary lung cancers. L-AmB was administered by 1 hour single infusion at fixed doses of 100 mg, and it was administered from 10 to 25 hours before the surgery. The starting and the end points of infusion were noted, the same for arterial and vein ligatures, and the end point of pulmonary tissue sample collection. Moreover, 10 ml of blood sample at the artery closure were collected. L-AmB was assayed in blood and lung tissue by an HPLC validated method of Bekersky et all (Shimadzu LC-9A pump, SPD-6A detector, CR-4A data processor, Simmetry Shield RP8 water column).

The blood levels after 10 to 16 hours from the end of infusion (n°6) ranged from 3.4 to 2.1 mg/l-gr, while the tissue levels ranged from 0.9 to 1.59 mg/l-gr; 18 to 22 hours after blood infusion (n°6) levels ranged from 1.8 to 0.9 mg/l-gr; 23 to 25 hours after infusion (n°6) blood and the tissue levels ranged from 1.8 to 0.98 mg/l-gr and 1.48 to 2.38 mg/l-gr. The tissue penetration shows fugicidal concentration.

These data support the consistent lung tissue diffusion of L-AmB in patients with primary and secondary lung cancers. The L-AmB plasma concentration was gradually decreasing in all the cases. The relationship between these data can effort the best choice of drug in possible fungal infections as for a prophylactic employment for lower dosage, inexpensive cost and for lower collateral side effects.