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Comparison of the pharmacokinetics of paracetamol from two generic products in patients after total gastric resection

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Abstract:
Gastrectomy leads to pathophysiological changes within the alimentary tract, which may affect drug absorption and pharmacokinetic parameters (PK). The need to apply orally administered analgesics in this group of patients is often related with alternative application of currently available generic products. Thus, from the clinical point of view it is necessary to evaluate the PK of these drugs to confirm their equivalence. The aim of the study was therefore an analysis of the pharmacokinetics of paracetamol from two generic products in patients after total gastric resection. The research was carried out on two groups of patients after gastrectomy with Roux-en-Y reconstruction (n = 30; mean [SD] age, 63.0 [11.5] years; weight, 67.6 [13.7] kg; and height, 166.4 [9.1] cm). The patients received paracetamol in a single orally administered dose of 1,000 mg. Blood samples were collected within 6 h of drug administration. The concentration of paracetamol and paracetamol glucuronide in the blood plasma was marked by means of a validated high-pressure liquid chromatography with ultraviolet detection (HPLC-UV). The main PK for paracetamol in group 1 (n = 17) and 2 (n = 13) were as follows: C_{max}, 9.46 (3.66) and 12.79 (5.32) μg/ml, respectively (p = 0.0517); $AUMC_{0-t}$, 77.64 (30.37) and 51.01 (15.76) μg h^2/ml (p = 0.0046); AUC_{0-inf}, 41.61 (23.52) and 30.28 (9.74) μg h/ml (p = 0.0862); t_{max}, 1.68 (0.63) and 0.50 (0.25) h (p < 0001). The obtained C_{max} and AUC values in patients after gastrectomy were reduced in comparison with healthy subjects. Total gastrectomy therefore affected the pharmacokinetics of paracetamol administered in tablets. In our patients, we also observed significant differences between the PK of paracetamol and two generic preparations. These two drugs can thus be used interchangeably, but with caution.

Key words:
paracetamol, tablets, gastrectomy, pharmacokinetics