EFFECT OF EXPERIMENTAL DIABETES ON PHARMACOKINETIC PARAMETERS OF LIDOCAINE AND MEGX IN RATS

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The aim of the study was to evaluate the effect of experimental diabetes on pharmacokinetic parameters of lidocaine and its metabolite monoethylglycylxylidide (MEGX) after a single intravenous administration in rats. The study was performed on male Wistar rats, randomized into 2 groups: group I – control animals and group II – animals with experimental diabetes induced by streptozotocin. Evaluation of lidocaine pharmacokinetics was performed 10 days after streptozotocin administration. Lidocaine concentrations were lower in rats with experimental diabetes compared with the values in the control group. In rats with diabetes, the shorter phase of distribution and faster drug elimination has been observed.

During the pharmacokinetic study, the dynamic reduction of lidocaine concentration was accompanied by the increase in MEGX concentration in blood. Drug elimination rate constant ($\lambda_2$) increased by 68% in rats with experimental diabetes which had an effect on the shortening of lidocaine half-life in those animals ($t_{1/2}$ by 39%) and on the increase in absolute clearance (CL) to 1.46 l/h comparing to control group (0.95 l/h), i.e. by 54%. The distribution rate constant of lidocaine ($\lambda_1$) was significantly greater in the animals with experimental diabetes (by 138%). The volume of distribution (Vd) in those animals decreased by 30% in comparison with the control group. The area under the plasma concentration-time curve (AUC) decreased by 48% in rats with experimental diabetes. The MEGX half-life ($t_{1/2}$) increased from 0.34 h in the control group to 0.89 h in the rats with diabetes, i.e. by 165%. It reflects the impaired MEGX elimination in experimental diabetes. The results suggest that experimental diabetes can have an effect on lidocaine pharmacokinetics towards enhanced lidocaine elimination with accompanied increase in its metabolite (MEGX) concentration.

Key words: lidocaine, MEGX, diabetes, pharmacokinetics

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