リノレン酸を取り込ませた培養肝細胞における パラコートの脂質過酸化作用

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High Susceptibility to Paraquat-Driven Lipid Peroxidation of Cultured Hepatocytes Loaded with Linolenic Acid

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Rat hepatocytes cultured without (normal cells) and with 1mM linolenic acid–bovine serum albumin complex for 12h were challenged with paraquat. The addition of paraquat to normal hepatocytes induced a relatively low level of lipid peroxidation even at the high concentration which caused severe cell injury. LNA-loaded hepatocytes markedly underwent lipid peroxidation on addition of paraquat, with a rise in the MDA accumulation beginning at the lowest concentration used. The enhanced lipid peroxidation in LNA-loaded hepatocytes was accompanied by the occurrence of cell injury at noncytotoxic parauat concentrations for normal cells. Of further importance was that in LNA-loaded cells, lipid peroxidation promptly occurred after the addition of paraquat and was followed by the loss of cell viability. Addition of antioxidants with paraquat prevented lipid peroxidation in both normal and LNA-loaded hepatocytes but protected only the latter cells from cell injury. Neither lipid peroxidation nor cell injury in either group of hepatocytes was prevented by the presence of •OH scavengers. In addition, paraquat-driven lipid peroxidation in LNA-loaded hepatocytes was promoted by the addition of ascorbate but was rather suppressed by the addition of H_2O_2.

In conclusion, it is likely that the addition of paraquat induced Fe^2-lipid

hydroperoxide-dependent lipid peroxidation that led to lethal cell injury in LNA-loaded hepatocytes.

培養肝細胞にリノレン酸を取り込ませることにより、薬物の脂質過酸化に対する感受性を増大させた脂肪肝細胞を用いて、パラコートの細胞傷害発現の機序の解明を試みた。本モデル細胞においてはパラコートによる細胞障害の発現に脂質過酸化が大きく関与していることが明らかにされた。