培養ラット脂肪肝細胞におけるパラコートの細胞障害作用

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Paraguat-Induced Oxidative Injury in Cultured Rat Lipidic Hepatocytes.

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Rat hepatocytes cultured for 12 h without (normal cells) and with 1.0 mM LMA-BSA (lipidic cells) were exposed to paraquat at concentrations of 0.05 to 1.0 mM. Normal heopatocytes underwent little lipid peroxidation as estimated the production of marondialdehyde (MDA) even with the addition of the highest concentration of 1.0mM paraquat to the cell cultures. In contrast, lipid peroxidation was provoked to a grest extent from 0.05 mM paraquat in the lipidic cells. The enhanced lipid peroxidation was followed by cell injury which was evaluated by a release of lactic dehydrogenase in association with a decrease in intracellular levels of glutathione and protein thiols in the lipidic cells. The presence of the antioxidants *N,N*-diphenyl-*p*-phenylenediamine, promethazine and γ-tocopherol in the culture medium prevented both lipid peroxidation and cell injury in the lipidic cells, but only lipid peroxidation in the normal cells. The effct or other unsaturated fatty acids on the enhancement of paraqut-induced lipid peroxidation and cellular injury was also examined. The potency of enhancing the deleterious effects of paraquat was related to the number of double bonds of the fatty acids.

初代培養ラット肝細胞に、リノレン酸を取り込ませて脂肪肝細胞を作製し、パラコートの細胞障害作用について、脂質過酸化に焦点をあてて調べた。培養脂肪肝細胞にパラコートを作用させると、正常肝細胞においては全く毒性を発現さない低濃度のパラコートで激しく脂質過酸化が誘起され、この脂質過酸化に伴って細胞障害も惹起された。プロメタジン、V・E、DPPD等の抗酸化剤は、脂肪肝細胞においてパラコート

が誘発した脂質過酸化と細胞障害を共に、効果的に抑制した。

パラコートが誘発するこの酸化的ストレスは、二重結合が数が多い脂肪酸を取り込んだ脂肪肝細胞おいてほど、強力に惹起された。