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Ursodeoxycholic Acid Improve The Cholangiocyte Differentiation And Favors Biliary Stones Dissolution

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Background : Cholangiopathies are increasingly recurrent and popular in people with liver diseases. Liver transplantation is undoubtedly the main treatment for these pathologies. Artificial bile duct has been regarded as an alternative and several reports have been published. However, a recurring phenomenon after surgery is the appearance of biliary stones, particularly pigment stones. For this reason, we try to reduce the incidence of biliary stone formation after replacement of artificial bile duct. We test several drugs and select ursodeoxycholic acid (UDCA) to prevent or minimize the generation of stones in the artificial bile duct.

Methods : Human gallbladder stones were tested with different drugs including UDCA to evaluate their dissolution power. Pigment, cholesterol and mixed stones were treated with several drugs for several days to check their size reduction. Poly vinyl ethanol nanofibers were covered with UDCA for its gradual release into an aqueous medium. The human chemically derived hepatic progenitor cells (hCdHs) were differentiated into cholangiocytes (hCdH-Chols) and seeded on the nanofibers.

Results : Compared to other drugs, UDCA showed the highest levels of dissolution at 120 h, which was reflected by the size of the stones. After this, the same procedure was carried out with cholesterol and mixed stones. UDCA showed similar effects, however its efficiency was lower and over a longer period of time. The hCdHs were seeded on UDCA-coated nanofibers and differentiated into cholangiocytes, the presence of UDCA favored differentiation of hCdHs to cholangiocytes.

Conclusions : As a preliminary study, UDCA showed the most effective dissolution of gallbladder stones, especially in the pigment stones. Furthermor, UDCA-coated nanofiber benefits cholangiocellular differentiation from hCdHs in vitro. These findins indicated UDCA is one of the most available drugs which can be used for the generation of drug eluting artificial bile duct. This work was supported by Korean Fund for Regenerative Medicine funded by Ministry of Science and ICT, and Ministry of Health and Welfare (21A0401L1) and National Research Foundation of Korea (2022R1F1A1073058).

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