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Introduction and Objectives: Hepatic cells undergo different processes in response to the steatogenic input of MAFLD. Hepatic cell culture in steatogenic medium is a useful, reproducible tool intended to elucidate these pathogenic mechanisms. This study aimed to study cellular proliferation, death, and senescence in hepatocytes and hepatic stellate cells (HSC) using a model of steatosis *in vitro*.

Materials and Methods: HepG2 hepatocytes were cultured in RPMI1640 (Control-Hep) and LX-2 HSC in DMEM (Control-LX2). Steatogenic media: either RPMI1640 or DMEM supplemented accordingly: *mild steatosis* (MS:50μM sodium oleate/sodium palmitate (OA/PA) at 2:1 ratio), *severe steatosis* (SS:500μM 2OA:1PA). HepG2 or LX-2 cells were preincubated for 24h at 37°C and 5% CO_2, then incubated in MS or SS medium for up to 72h. Steatogenic medium was refreshed daily. Viability, mortality, proliferation, and senescence were analyzed. Assays are performed in triplicates. Data: Mean±SD. 2-way ANOVA followed by Tukey. $P<0.05$.

Results: Hepatocytes: MS showed lower viability and proliferation, with increased mortality at 72h and higher senescence from 48h. SS displayed lower viability, and proliferation, with increased mortality but lower senescence from 24h. HSC: MS showed diminished viability and increased mortality (16.0%) at 72h. SS showed lower viability and increased mortality rate (50.0%) from 48h.

Proliferation increased in both MS and SS at 24h but decreased by 72h. Cellular senescence was diminished at 24 and 48h in both steatogenic conditions.

Conclusions: Steatogenic conditions induced different outcomes in the two cell lines studied. Hepatocyte behavior depends on lipid contents. In MS, increased senescence might be considered a mechanism to avoid damaged-cell proliferation. In SS, increased mortality rate and decreased senescence suggest lipotoxicity and activation of death pathways. In contrast, HSC cultured in steatogenic conditions might turn into the activated state, therefore increasing their proliferation and avoiding other cellular processes, including senescence. Both hepatocyte and HSC outcomes presented here contribute to the pathogenesis of MAFLD.

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P- 28 ATORVASTATIN SHOWS ANTI-PROMOTOR AND ANTI-NEOANGIOGENIC EFFECT IN HEPATOCELLULAR CARCINOMA DEVELOPMENT IN VIVO AND IN VITRO MODEL BY INHIBITING TGF-β1/pERK SIGNALING PATHWAY

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Introduction and Objectives: Hepatocellular carcinoma (HCC) represents 90% of liver tumors. Statins may reduce HCC incidence. Its antitumor activities are controversial and may be mediated by disrupting several hepatocarcinogenic pathways. This study aimed to evaluate *in vivo* and *in vitro* the anti-proliferative and anti-angiogenic action of atorvastatin (AT) in the development of HCC as well as its mechanisms of action.

Materials and Methods: *In vivo* model: the pesticide hexachlorobenzene (HCB) was used to promote the development of HCC in Balb/C nude mice inoculated with Hep-G2 cells. Tumor hepatic number, cell proliferation parameters (proliferating cell nuclear antigen, PCNA), cholesterol metabolism (3-hydroxy-3-methylglutaryl-coenzyme-A-reductase, HMGCoAR), angiogenesis and VEGF levels were analyzed. *In vitro* model: Hep-G2 and Ea-hy926 cells were used to evaluate the effect of AT (2,5; 5 and 5 mg/kg b.w.) on HCB-induced cell proliferation, migration, and vasculogenesis and analyze proliferative parameters.

Results: *In vivo*: AT 5 mg/kg prevented liver growth and tumor development and inhibited PCNA, TGF-β1 and pERK levels increase. AT 5 mg/kg prevented VEGF levels and skin blood vessel formation. *In vitro*, AT prevented cell proliferation and migration as well as tubular formation in the endothelial cell line by inhibiting the TGF-β1/p ERK pathway.

Conclusions: We were able to demonstrate the potential AT antiproliferative and anti-angiogenic effects in an HCC model and the involvement of TGF-β1 and pERK pathways.

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P-29 THE LIVER IN AMYLOIDOSIS: AN ANALYSIS OF THE INSTITUTIONAL AMYLOIDOSIS REGISTRY

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Introduction and Objectives: The liver can be either compromised by infiltrative damage of amyloid, as it happens in AL and AA amyloidosis, or its cause, as it occurs in transthyretin TTR-related amyloidosis. In the latter, the liver synthesizes a defective variant TTR which has the capacity for cardiac, neurological, and renal damage, but the liver function is preserved. This study aimed to describe the clinical characteristics and prognosis of patients with liver involvement of amyloidosis (AL and AA)

Materials and Methods: Retrospective cohort of patients with hepatic involvement included in the Institutional Amyloidosis Registry (ClinicalTrials.gov NCT01347047) between June 2010 and January 2022. Clinical characteristics and complementary studies were analyzed, as well as their evolution.