combination therapy. Comprehensive molecular characterization included RNA sequencing with subsequent differential gene expression analysis, pathway enrichment studies, and protein interaction network mapping. Mechanistic findings were confirmed through immunohistochemical and immunoblotting techniques.

Results: The SB-SF combination demonstrated enhanced anticancer efficacy compared to SB alone. Transcriptomic profiling identified 45 differentially expressed genes associated with HCC suppression, particularly those involved in proliferation control, oxidative stress response, and apoptotic regulation. The combination therapy significantly downregulated key oncogenic markers including NF-κB-p65, COX-2, and β-catenin, suggesting its potential as a cost-effective therapeutic approach that warrants further clinical investigation.

Conclusions: The study reveals a multifaceted mechanism by which SF augments SB's anticancer activity in HCC. The combined treatment modulates critical oncogenic pathways including NF-κB and Wnt/β-catenin signaling while rebalancing apoptotic regulators through decreased Bcl-2 and increased Bax/caspase expression. Additionally, it suppresses proliferative markers such as Ki-67 and PCNA while attenuating inflammatory mediators including TNF-α and MMP-9. These coordinated effects demonstrate potent anti-tumorigenic, anti-angiogenic, and pro-apoptotic activity, highlighting the therapeutic promise of this combination approach for HCC treatment.

Conflict of interest: None

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#20

CONNECTIVE TISSUE GROWTH FACTOR AS A MARKER OF FIBROSIS IN PATIENTS WITH CHOLESTASIS

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Introduction and Objectives: Connective Tissue Growth Factor (CTFG) is a multifunctional protein, plays a crucial role as a mediator in fibrogenic pathways involved in the development and progression of liver disease.

To establish the correlation between serum CTGF values by ELISA and the degree of liver fibrosis determined by transitional elastography in patients with cholestasis diagnosed with primary biliary cholangitis (PBC).

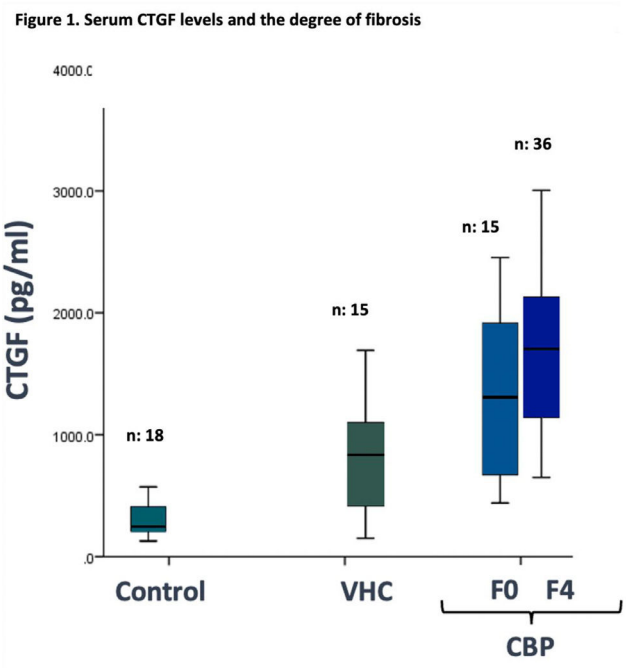
Materials and Methods: A descriptive and analytical prolective study that included patients with cholestasis diagnosed with PBC, patients with cirrhosis due to hepatitis C and a control group of healthy subjects. Serum CTGF levels and the degree of fibrosis were quantified. Statistical analysis: CTGF means were compared using a univariate model with etiology as an between-group factor and degree of fibrosis as an within-group factor, significance level 5%.

Results: 51 patients with PBC, 15 HCV and 18 controls were included. Age 48±15 years, 75% women. The level of CTFG in patients with cholestasis increased with increasing degree of fibrosis. PBC (F0) 1342.4±669.9; PBC (F4) 1679.9±623.3. HCV (F4) 816.3±431.6, CT 314.1±163. Statistically significant differences (p<.001) were found between groups CT vs PBC (F0); CT vs CBP (F4), HCV (F4) vs PBC (F4) and CT vs HCV (F4). Figure 1

Conclusions: There is a direct relationship between serum levels of CTFG of patients with cholestasis and degrees of fibrosis by transition elastography, perhaps it can be considered as a marker of fibrosis induction in patients with cholestasis.

Conflict of interest: None

Serum CTGF levels and the degree of fibrosis



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#21

CONNECTIVE TISSUE GROWTH FACTOR ASSESSMENT: DETERMINATION OF CUT-OFF POINTS FOR LIVER FIBROSIS IN CHOLESTASIS

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Introduction and Objectives: Connective Tissue Growth Factor (CTFG) is a multifunctional protein, plays a crucial role as a mediator in fibrogenic pathways involved in the development of liver disease. Objective: To establish the correlation between the cut-off point of serum CTGF values by ELISA and the degree of liver fibrosis determined by transitional elastography in patients with cholestasis diagnosed with primary biliary cholangitis (PBC).

Materials and Methods: Prolective, descriptive and analytical study, which included patients with cholestasis, with cirrhosis due to hepatitis C and a control group. Serum CTGF levels were quantified in blood. The degree of fibrosis was determined by transitional elastography. The AUROC was calculated and the cut-off point was obtained with the Youden index to obtain sensitivity and specificity, between CT vs HCV-F4, CT vs CBP-F0, CT vs CBP-F4 and HCV-F4 vs CBP-F4.

Results: 51 patients with PBC, 15 HCV and 18 controls were included, Age 48±15 years, 75% female.The AUROC for HCV-F4 vs TC was .856 (.718-.994, CI95%) p<.001, cutoff 592.9, S=66.7%, E=94.4% for TC vs PBC-F0 was AUROC=.974 (.929-1.0,CI95%) p<.001, cutoff=596.18, S=93.3%, E=94. 4%, for TC vs PBC-F4 was AUROC=.997 (.989-1.0, CI95%), p<.001, S=100, E=94.4%, for HCV-F4 vs PBC-F0 was AUROC=.857 (.769-.956, CI95%), p<. 001, cut-off=1284.7, S=69.4%, E=93.3% and for HCV-F4 vs PBC-F4 was AUROC= .738 (.557-.918,IC95%), p=.026, cutoff=1288.6, S=53.3%, E= 93.3%.

Conclusions: There is a direct relationship between serum levels of GFRT of patients with cholestasis and specific cut-off points of discrimination for the different groups.

Conflict of interest: None

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#22

EVALUATION OF RESPONSE TO SECOND LINE THERAPY IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS AND INADEQUATE RESPONSE TO UDCA: A PILOT STUDY OF LIVER BIOPSIES FOLLOW UP

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Introduction and Objectives: Response to second line therapy is improvement of cholestatic parameters and prevention of fibrosis or liver events. AIM: to evaluate response at Month 12 and identify epidemiological, clinical and histological findings related to response.

Patients and Methods: 50 patients initiating OCA (n=12), PPAR agonists (n=29) or combination of both (n=9) completed 12 months treatment and had baseline and M12 biopsy. Duct loss was evaluated with cytokeratin 7 and 19 and Scheuer staging applied. Biliary interface activity and bile duct damage recorded. Elastography was done at baseline and at 12 months. Statistical analysis using parametric t tests and 1-way ANOVA was performed.

Results: Mean age 53.6±10.6y and 84 % female. Mean ALP 388.8± 166.6, ALT 71.3±40.6 and BT 0.9±0.4. 10 patients were cirrhotic. Response to second line therapy was 30 % with POISE criteria (n=15) and 14 % for ALP normalization (n=7). Male sex (p.04), moderate/severe ductopenia (p.01), elevated ALT (82 vs 46, p.003), bilirubin (1.07 vs 0.7, p.02) and cirrhosis (p.02) correlated with no response. Moderate/severe portal inflammation with interface hepatitis and lobular spilling was observed in 28 samples, irrespective of age and correlated with fibrosis. No patient with severe inflammation achieved response (n=5), and only 21% with moderate inflammation (n=5). On FU biopsies, response related with improvement of inflammation in 11 patients. Mild ductopenia did not affect response. No LFT predicted cirrhosis or portal inflammation. Cirrhosis at month 12 correlated with liver events in 5 patients resulting in 1 liver related death and 3 transplants. Elastography correlated with cirrhosis and liver events (10.4 vs 22.9, p<0.001) but not with inflammation or ductopenia.

Conclusions: Non response (70 %) related to male sex, cirrhosis, transaminases, moderate/severe inflammation and ductopenia. Cirrhosis and elastography correlated with liver events. Adverse histological findings suggest early second line intervention.

Conflict of interest: None

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#24

CORE MUTATIONS IN THE HBEAG-NEGATIVE STAGE ARE KEY DETERMINANTS OF HEPATITIS B VIRUS REPLICATION

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Introduction and Objectives: The natural history of chronic HBV infection is characterized by distinct stages resulting from virus-host interactions. In this context, a late and pivotal event is HBeAg seroconversion, marked by the abrogation of HBeAg expression, a significant reduction in viral load, and the accumulation of mutations throughout the genome. While HBeAg abrogation is associated with mutations in the BCP and preCore regions, these mutations do not, per se, account for the observed reduction in viral load. Our aim was to unravel, at the molecular level, the drivers involved in the HBV replication rate.

Materials and Methods: Full-lenght HBV genome obtained from plasma samples of one HBeAg-positive patient and three HBeAg-negative patients was extracted, amplified and cloned. The replicative capacity and HBsAg antigen expresion of these clones and the chimeras obtained through core gene exchanges was evaluated in vitro.

Results: The incorporation of the wild-type (WT) core protein into HBeAg-negative genomes restored all viral replication intermediates (cccDNA, pgRNA, rcDNA, and capsid-associated DNA) to levels comparable to those of the WT virus and vice versa (Figure 1). Furthermore, a regulatory role of mutations in the core protein was observed in the modulation of HBsAg expression and secretion (Figure 2).

Conclusions: HBV viral load is a critical factor in the progression of chronic hepatitis B and its associated adverse outcomes. Mutations identified subsequent to HBeAg seroconversion are frequently found within the core region, and these mutations demonstrate a strong association with both HBV-DNA replication capacity and HBsAg expression levels.

Conflict of interest: None