

## البحث الثامن:

عنوان البحث باللغة الانجليزية:

Combined effect of hydrogen sulfide and mesenchymal stem cells on mitigating liver fibrosis induced by bile duct ligation: Role of anti-inflammatory, anti-oxidant, anti-apoptotic, and anti-fibrotic biomarkers

## Article 8

Objective(s): Liver fibrosis eventually develops into cirrhosis and hepatic failure, which can only be treated with liver transplantation. We aimed to assess the potential role of hydrogen sulfide (H<sub>2</sub> S) alone and combined with bone marrow-derived mesenchymal stem cells (BM-MSCs) on hepatic fibrosis induced by bile-duct ligation (BDL) and to compare their effects to silymarin. Materials and Methods: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TB), and alkaline phosphatase (ALP) were investigated in serum. Gene expression levels of CBS (cystathionine  $\beta$ -synthase), CSE (cystathionine  $\gamma$ -lyase), and alpha-smooth muscle actin ( $\alpha$ -SMA) were measured in liver tissues using RT-PCR. Hepatic protein kinase (Akt) was assessed by Western blot assay. Liver oxidative stress markers, malondialdehyde (MDA), and reduced glutathione (GSH) were analyzed by the colorimetric method. Lipocalin-2 (LCN2) and transforming growth factor- $\beta$  (TGF- $\beta$ ) were measured using ELIZA. Liver tissues were examined by H&E and Masson trichome staining for detection of liver necrosis or fibrosis. Caspase 3 expression was evaluated by immunohistochemistry. Results: H<sub>2</sub> S and BM-MSCs ameliorated liver function and inhibited inflammation and oxidative stress detected by significantly decreased serum ALT, AST, ALP, TB, and hepatic MDA, Akt, TGF- $\beta$ , LCN2, and  $\alpha$ -SMA expression and significantly increased CBS and CSE gene expression levels. They attenuated hepatic apoptosis evidenced by decreased hepatic caspase expression. Conclusion: Combined treatment with H<sub>2</sub> S and BM-MSCs could attenuate liver fibrosis induced by BDL through mechanisms such as anti-inflammation, anti-oxidation, anti-apoptosis, anti-fibrosis, and regenerative properties indicating that using H<sub>2</sub> S and MSCs may represent a promising approach for management of cholestatic liver fibrosis.

