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Ain Shams University
Women's College for Arts
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Effect of Stem Cells on Chromosomal Abnormalities Induced by CCl₄ in Experimental Rat Liver Fibrosis

Thesis

Submitted to Women's College, Ain Shams University
For Ph.D. Degree in Science

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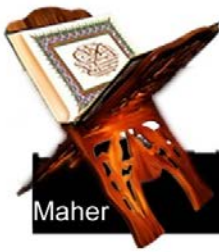
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ABSTRACT

Regenerative medicine is a novel field that utilizes stem cells for the restoration of damaged tissues and improvement of organ functions. So, this study aimed to estimate and compare the possible therapeutic role of rat mesenchymal stem cells (MSCs) and human CD34⁺ stem cells in the amelioration of liver fibrosis and chromosomal abnormalities induced by carbon tetrachloride (CCl₄). Male albino rats were divided into 4 groups: control, CCl₄, CCl₄ plus MSCs, and CCl₄ plus CD34⁺. The fibrosis was induced by using subcutaneous route injection of CCl₄ at a dose of 0.2 mL/100 g body weight twice a week for 6 weeks. After 6 weeks of CCl₄ administration, stem cells (MSCs and CD34⁺) were given as a single dose of 10⁷ cells per rat and left for one month. The liver tissues, blood and bone marrow samples were collected from rats to assay the following parameters: type 1 collagen and metalloproteinase (MMP)-2 gene expressions in liver tissues, biochemical analysis of albumin and alanine aminotransferase (ALT) levels in serum, histopathological and immunohistochemical examinations for liver tissues, and cytogenetic analysis for bone marrow cells. The results showed that, CCl₄ administration induced many histological alterations and the fibrosis was the most prominent type of alterations

observed. Also, CCl₄ administration significantly increased (P<0.05) immunopositivity of cells toward α -smooth muscle actin (SMA) antibody, type 1 collagen and MMP-2 gene expressions. There was also a significant decrease (P<0.05) in serum albumin level and a significant increase (P<0.05) in serum ALT level and also chromosomal aberrations in bone marrow cells of rats after CCl₄ administration. Regards to the two types of stem cells the results stated that, treatment with multipotent stem cells (MSCs and CD34⁺) decreased the fibrotic tissue and improved liver tissue architecture in rats affected with liver fibrosis. Also they reduced the percentage of α -SMA-positive cells and significantly decreased (P<0.05) type 1 collagen and MMP-2 gene expressions in liver tissues that induced by CCl₄. The results also showed a significant elevation (P<0.05) in serum albumin after administration of both types of stem cells, but ALT level and chromosomal aberrations in bone marrow cells were significantly decreased (P<0.05) only in CCl₄/CD34⁺ group while in CCl₄/MSCs group they were slightly decreased. In conclusion, the two used types of stem cells have a potential effect in the improvement of hepatic injury and mitigation of the chromosomal abnormalities induced by CCl₄.

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