عنوان مقاله:

Bone Marrow-Derived Mesenchymal Stem Cells and Pioglitazone or Exendin-۴ Synergistically Improve Insulin Resistance via Multiple Modulatory Mechanisms in High-Fat Diet/Streptozotocin-Induced Diabetes in Rats

محل انتشار:

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نویسندگان:

.Mohamed Mohamed Mesbah - *Biochemistry Department, Faculty of Science, Ain Shams University, Cairo, Egypt*

.Laila Ahmed Rashed - *Department of Medical Biochemistry, Faculty of Medicine, Cairo University, Cairo, Egypt*

.Noha Ahmed El-Boghdady - *Department of Biochemistry, Faculty of Pharmacy, Cairo University, Cairo, Egypt*

.Mahmoud Mohamed Said - *Biochemistry Department, Faculty of Science, Ain Shams University, Cairo, Egypt*

خلاصه مقاله:

Background: Diabetes mellitus (DM) is a metabolic disease, characterized by hyperglycemia resulting from defects in insulin secretion and/or insulin action. The current study was designed to assess the therapeutic potential of bone marrow-derived mesenchymal stem cells (BM-MSCs) alone and in combination with pioglitazone (Pz) or exendin-۴ (Ex) in high-fat diet/streptozotocin (HFD/STZ)-induced diabetes in rats. Methods: The rats were subjected to the HFD for three weeks before being injected with a single low dosage of STZ (۳۵ mg/kg bw). The animals were assigned to different treatment groups after type II diabetes mellitus (T۲DM) induction was confirmed. Results: Severe insulin resistance was verified in untreated HFD/STZ T۲DM rats, along with the exaggeration of oxidative stress, inflammation, apoptosis, and autophagy suppression in the adipose tissues. Monotherapy of HFD/T۲DM rats with BM-MSCs and Pz or Ex alleviated diabetic complications by increasing insulin sensitivity, decreasing apoptosis and inflammation as evidenced by a decrease in serum tumor necrosis factor-alpha, caspase-۳, and nuclear factor-kappa B (NF-kB) genes expression and Janus kinase (JNK) protein expression, and enhancing autophagy as revealed by upregulation in beclin and LC۳, as well as peroxisome proliferator-activated receptor-g coactivator-۱ alpha (PGC-۱α) genes expression in the adipose tissues. An augmented ameliorative efficacy was recorded in combined treatments. The biochemical and molecular results were confirmed by histological investigation of pancreatic tissues. Conclusions: Combining Pz or Ex with BM-MSCs is a synergistic therapeutic option that reduces insulin resistance and subsequent complications in T۲DM via multiple molecular mechanisms.

کلمات کلیدی:

.Exendin-۴, High-fat diet, Mesenchymal stem cells, Pioglitazone, Streptozotocin, Type II diabetes mellitus