Ebselen Rescues High Glucose Suppressed Osteogenic Differentiation of BMSCs by the Activation of PI3K/AKT Pathway

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Background

Patients with diabetes mellitus often have high risk of titanium implant failure due to compromised bone regeneration ability. It has been demonstrated that the poor osteogenic ability is partly due to high glucose induced excessive oxidative stress. To date, specific treatments for these patients are needed. Ebselen, a non-toxic organoselenium compound, is been reported to be a potent antioxidant agent. However, few studies have yet investigated the effects of ebselen on osteogenic differentiation of bone marrow-derived mesenchymal stem cells (BMSCs) under high glucose.

Aim

The aim of this study was to evaluate the influence of ebselen on BMSCs under high glucose condition and explore the underlying mechanism.

Methods and Materials

BMSCs were isolated from SD rats and their morphology and multiple differentiation abilities were characterized. BMSCs were divided into 3 groups including: normal glucose (5.5mM) group (control), high glucose (25.5mM) group, high glucose group supplemented with 10 μ M ebselen group. The proliferation rates, alkaline phosphatase (ALP), alizarin red staining, osteogenic-related protein levels and intracellular reactive oxygen species (ROS) generation were evaluated. Western blot was also performed to investigate the role of PI3K/AKT pathway.

Results

1. Characterization of BMSCs and ebselen promoted BMSCs proliferation under high glucose

Fig.1 (A) Characterization of BMSCs. (B) Proliferation rates of BMSCs under different culture conditions

2. Ebselen increased ALP activity and calcium deposition of BMSCs under high glucose

Fig.2 Mineralization and ALP activity of BMSCs under high glucose

3. Ebselen enhanced osteogenic-related protein expression of BMSCs under high glucose

Fig.3 The effect of ebselen on expression levels of osteogenic-related proteins

4. Ebselen decreased ROS production of BMSCs under high glucose

Fig. 4 Effect of ebselen on intracellular reactive oxygen species (ROS) production in BMSCs culturing with high glucose

5. The effect of ebselen in promoting BMSCs osteogenic differentiation under high glucose was abolished by inhibition of the PI3K/Akt pathway

Fig.5 Runx2 and p-Akt expression levels were determined after incubating with or without ebselen and Akt inhibitor

Conclusion

Ebselen could attenuate osteogenic dysfunction of BMSCs induced by high glucose through an-antioxidant effect and the activation of the PI3K/Akt pathway, suggesting that ebselen have potential therapeutic effect for patients with diabetes mellitus to combat bone regeneration dysfunction.

References

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