THE EFFECT OF UMBILICAL CORD STEM CELLS ON ISOPROTERENOL - INDUCED MYOCARDIAL INFARCTION IN ALBINO RATS; HISTOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY

Thesis

submitted for partial fulfillment of M.D. degree in Histology

Presented by

Doaa Ibrahim El Dosoki Mohamed

M.Sc

Under the supervision of

Prof. Dr. Nagwa Abdel Wahab Ahmed

Professor of Histology, Faculty of Medicine,

Cairo University

Prof. Dr. Dina Helmy Mohammed

Professor of Histology, Faculty of Medicine,

Cairo University

Dr. Mohamed Salah Elgendy

Assistant Professor of Histology, Faculty of Medicine,

Fayoum University

Department of Histology

Faculty of Medicine

Fayoum University

2015

Summary and Conclusion

Myocardial infarction (MI) is a major public health problem and the leading cause of mortality in both developed and developing countries. patients with severe heart failure require invasive treatment such as mechanical circulatory support, continuous inotropic infusion, or cardiac transplantation. However, the search for compatible donors and immune suppression limit the application of this procedure and alternative therapies are needed. For these reasons, cell transplantation is considered as a promising therapeutic approach for MI in both laboratory studies and clinical trials.

This work aimed at investigating the role of mesenchymal stem cells from umbilical cord blood in the treatment of experimentally-induced myocardial infarction in male albino rats. Histological and immunohistochemical technique in addition to morphometric measurements and statistical analysis of the data were used in this study.

Fourty male albino rats were used and divided into

Group I: eight healthy rats served as **control group**

Group II (MI group): 24 rats were MI was induced. After induction of MI by subcutaneous injection with 100 mg/kg isoproterenol daily for two days, the rats of this group were subdivided according to time of sacrifice into the following subgroups:

group II_{d1}: eight rats, time of sacrifice one day after induction of MI.

group II_{d3}: eight rats, time of sacrifice three days after induction of MI.

group II_{d40}: eight rats, time of sacrifice forty days after induction of MI.

Group III(MI + stem cells group): eight rats, 10 days after induction of MI, were injected with 500.000 stem cells suspended in 0.5 ml phosphate

buffer saline in caudal vein. Random sample of two rats were sacrificed after three days from stem cells injection to detect homing of stem cells by Prussian blue stain. Then, the rats were sacrificed after thirty days from stem cells injection.

The hearts were dissected and processed for paraffin blocks formation, sectioned and subjected to the following techniques Haematoxylin and Eosin stain, Prussian blue stain, Masson's trichrome stain, Immunohistochemistry technique using CD34 and troponin T antibodies, quantitative morphometric analysis and statistical analysis of the data.

In group II (MI group) there were destroyed, interrupted, separated, wavy and darkly eosinophilic cardiac muscle fibers with no cross striations or nuclei in many fibers, ghost and enlarged rectangular nuclei in other fibers, multiple vacuoles and contraction band necrosis also appeared, Vacuolated areas, dilated congested blood vessels, extravasted RBCs and cellular infiltration were present inbetween cardiac muscle fibers. There was collagen deposition inbetween cardiac muscle fibers and subendocardium confirmed by a significant increase in fibrosis expressed by high collagen area % when compared to control group. There was also a significant decrease in the percentage of healthy cardiac muscle expressed by troponinT area% when compared to control group.

In group III (MI + stem cells group), collagen deposition decreased inbetween cardiac muscle fibers and subendocardium as reflected by a significant decrease in fibrosis expressed by mean collagen area % when compared to MI group.There was increased neovascularisation detected by CD34 immunostain positive-endothelial cells lining many small blood vessels and confirmed by significant increase in CD34 area % when compared to MI groups. The cardiac muscle fibers appeared healthy with

normal arrangement and little interstitial spaces confirmed by a significant increase in the healthy cardiac muscle expressed by troponinT area% when compared to MI group.

Conclusion and recommendations

From the present study we can conclude that the mesenchymal stem cells extracted from umbilical cord blood have a potential role in the treatment of myocardial infarction through decreasing fibrosis and increasing neovascularization in and around the infarcted area which improve tissue perfusion , decrease apoptosis of hypertrophied myocytes, maintain survival of viable myocardium, reduce collagen deposition and improve cardiac function . Further researches are recommended to study the role of cord blood mesenchymal stem cells in treatment of MI infarction or other cardiac diseases in human.