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Improvement of Renal Failure Using Wharton's Jelly Derived Mesenchymal Stem Cells

Mohamed Ali[1], Nashwa M Barakat[2], James J Yoo[3], Sang Jin Lee[3], Anthony Atala[3], and Faten Zahran[1]

[1]Department of Chemistry, Faculty of Science, Zagazig University, Zagazig, Sharkia 44519, Egypt, [2]Urology and Nephrology Center, Mansoura University, Mansoura, Egypt 35516, [3]School of Biomedical Engineering and Sciences, Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA

Abstract

Introduction. Renal failure is one of the major health problems worldwide, dialysis and kidney transplantation are the only available therapies used in clinic. However, high cost and increasing demand with limited organ donor still provide challenges. An alternative therapeutic approach to the present treatment is the utilization of stem cells to treat kidney diseases owing to its high proliferation rate and multipotency. Additionally, stem cells possess anti-inflammatory and antioxidant effects, which in turn help in tissue repair by decreasing cell damage resulting from injury. The current study aims to evaluate the role of mesenchymal stem cells derived from Wharton's jelly tissue (WJMSCs), and hyaluronic acid (HA) in the restoration of kidney functions in acute renal failure model.

Methods. MSCs were enzymatically isolated from Wharton's jelly tissue and expanded *in vitro*. The isolated cells were then characterized to confirm their MSCs criteria. The therapeutic potential of WJMSCs both treated and untreated with HA was evaluated by injecting the isolated cells into the renal cortical region of ischemic renal failure model. Blood, urine, and tissue samples were collected for biochemical and histological measurement to assess the improvement of renal functions in all experimental groups.

Results. The results revealed that Wharton's jelly derived MSCs exhibit the general characteristic features of MSCs isolated from other sources. better renal function amelioration was observed in the treated groups compared to the positive control group. The utilization of hyaluronic acid along with WJMSCs enhance the ability of WJMSCs to repair the injured kidney tissue

Conclusions. In conclusion WJMSCs were able to restore the renal functions and prevent tissue damage after ischemia reperfusion injury. Furthermore, the utilization of HA increased the regenerative capability of WJMSCs.

Keywords: Regenerative Medicine, Renal Failure, Wharton' Jelly, MSCs, Hyaluronic Acid

Introduction

Kidney failure is a major health trouble facing several patients worldwide, with the only accessible treatments being dialysis and kidney transplantation. The current available medical therapies include kidney dialysis, which is non-curative and costly, and kidney transplantation, which is curative, however, risks organ rejection and there exists an organ shortage. An alternative treatment approach to kidney diseases is to utilize stem cells therapy. It has been speculated that stem cells are able to boost tissue repair in several experimental models via transdifferentiation, cell fusion, or paracrine effect through release of cytokines and growth factor, consequently stem cell therapies hold a promising option for regeneration of several organs, including kidneys [1-11].

Renal IR injury is a complex inflammatory process that may happen during kidney transplantation, partial nephrectomy, or renal vascular surgery and may result in rejection and/or delayed graft function. IR injury causes impairment of kidney function, which may be attributed to glomerular endothelial cell injury or tubular obstruction [12].

Stem cells are undifferentiated cells capable of give rise to more specialized cells, they are commonly derived from embryonic and adult sources. MSCs are the most major type of adult stem cells, they are located in several tissues and prominent in the bone marrow and umbilical cord [13]. The isolation of bone marrow derived MSCs requires invasive procedures and yields low quantity [14]. Thus, this study utilized MSCs isolated from Wharton's jelly tissue of the umbilical cord (WJMSCs) to treat renal ischemia reperfusion (IR) injury, due to WJMSCs properties, such as self-renewal,

Correspondence to: Mohamed Ali, Department of Chemistry, Faculty of Science, Zagazig University, Zagazig, Sharkia 44519, Egypt; Phone +1 336 4735735; E-mail: maali@wakehealth.edu; Mohamedali_eg@zu.edu.eg

high proliferation rate, multipotency, and their anti-inflammatory and antioxidant effects. Furthermore, they possess immunomodulatory properties, meaning they are able to reduce immunogenicity to avoid the risk of allogenic cell rejection by host tissue [15]. All these features allow these cells type to be used in clinical therapy. Hyaluronic acid (HA) is non-sulfated glycosaminoglycan and has a high molecular weight up to 20 MDa. HA is natural polysaccharide composed of repeating disaccharide units of N-acetyl glucosamine and glucuronic acid. HA is located in several tissues, including epithelial, neural, and connective tissues. HA also enhances cell proliferation, migration and homing. Furthermore, HA increases healing rate and decreases fibrosis, as well as regulates cell-cell and cell-matrix adhesion [16,17].

We hypothesize that WJMSCs help in restoring the kidney function after IR injury. Treatment of WJMSCs with HA enhances cell proliferation and homing in injured tissues, thus increasing its reno-protective function. First, we aimed to isolate MSCs from tissue and evaluated their features and their ability to restore the kidney function in a renal failure model. Second, we investigated the effect of HA treatment on the maturation and differentiation of WJMSCs. We evaluated the improvement of renal function of rats with kidney disease through blood chemistry for creatinine, BUN, and creatinine clearance analysis and histological examination.

- **Experimental Design**
- **Isolation and characterization of Wharton' Jelly Mesenchymal stem cells**
- **Umbilical cord collection and Cell isolation**

Umbilical cords were collected from healthy, full-term deliveries rapidly after prior consent of the volunteers according to a policy approved by the IRB and Ethical Committee. The umbilical cord was rinsed with sterile phosphate buffered saline (PBS; PH 7.4) under aseptic technique to remove blood and other debris. The umbilical vein and arteries were dissected from Wharton's jelly tissue, then the tissue was chopped into small pieces ~2-3 mm^3 in size and collected into 50 ml sterile centrifuge tube. MSCs were enzymatically isolated from Wharton's jelly tissue using collagenase type I (Sigma Aldrich, SCR103) at a concentration of 1mg/ml for 1 hour at 37ºC under continuous shaking. The cells were obtained by centrifugation of the previous mixture for 10 min at 1500 rpm, after which the supernatant was discarded and the cell pellet was resuspended in complete growth medium composed of [DMEM high glucose, 10% fetal bovine serum FBS and 1% Penicillin/ Streptomycin] and cultured into 75 cm^2 flasks then incubated in CO2 incubator in humidified atmosphere at 37°C with 5% CO2. The media was changed twice per week. The cells were passaged when confluency reached 70-90 % by incubating with trypsin EDTA 0.25% for 3-5 min at 37 ^oC. The reaction was stopped by adding 5 ml of growth medium and the suspension was centrifuged at 1500 rpm for 5 minutes. The cell pellet was resuspended in complete growth medium and reseeded at ratio 1:3 [18].

Cell Growth and population doubling time (PDT)

A short-term cell growth assay was performed by seeding WJMSCs into 6 well plates at a concentration of 1×10^4 cells/well and incubating with growth media in CO_2 incubator. The cells detached at days 2, 4 and 7 and the cell numbers were counted to create a growth curve. Additionally, cell viability was assessed using Trypan blue exclusion test. To determine the population doubling times (PDT), MSCs were plated into 6 well plates at a concentration of 1×10^4 cells/well. When the cells reach 80-90% confluence, the cells were harvested, counted and reseeded at the initial density. This procedure was repeated every passage. PDT value was analyzed according to the following equation: where Tc is the culture time (hours), whereas N0 is the number of seeded cells and Nt represent the number of harvested cells [14].

Colony forming unit-fibroblast (CFU-F) assays

A CFU-F assay was used to evaluate the proliferation and colonogenic capacity of the MSCs expanded in culture. WJMSCs were seeded in triplicate at 5×10^3 concentration into 60 mm cell culture plate then incubated for 7-10 days at 37°C in 5% humidified CO_2 incubator, the cell monolayer was washed with PBS, fixed in ice cold methanol, and stained with 0.1% crystal violet solution for 10 min. Clones of more than 50 cells were scored as a colony forming unit-fibroblast [19].

Immunofluorescence staining

WJMSCs were characterized by immunofluorescent staining of cell surface marker Vimentin. WJMSCs at Passage 3 were seeded on a chamber slide (BD Falcon, USA) with growth medium and incubated overnight in CO_2 incubator. The cells were fixed with 4% para formaldehyde and permeabilized with 0.1% TritonX-100. Non-specific sites were blocked using Dako protein blocking solution, the cells were incubated with primary antibodies mouse anti-Vimentin (ab20346) using 1:100 dilution at 4^oC overnight, then incubated with secondary antibody goat anti-mouse IgG labelled with Alexa Fluor® 488 (ab150117) at 1:400 dilution for 1 hour at room temperature. Nuclear DNA was labelled in blue with DAPI stain. The images were taken using fluorescence microscope (Leica, Germany) [20].

Osteogenic Differentiation

WJMSCs were harvested at Passage 3 using Trypsin EDTA as previously described, then seeded in triplicate

into 6 well plate at a concentration of 5×10^4 cells per well, then divided into two groups; the first group was cultured in osteogenic differentiation media composed of [DMEM supplemented with 10% FBS, 0.1μM dexamethasone, 10mM β-glycerol phosphate and 50μM Ascorbic acid]. The second group was cultured with normal growth media and used as a control. The media was changed twice per week for 2 weeks. The differentiation potential of WJMSCs was assessed by Alizarin red stain and alkaline phosphatase (ALP) activity. For Alizarin red stain, the cells were fixed using 10% neutral buffered formalin and stain with Alizarin red dye. During this reaction, the dye reacts with the Ca^{2+} ion and gives a red color, after which the images were taken using inverted light microscope (Zeiss Axiovert, Germany). Additionally, the stain was quantitively analyzed spectrophotometrically by extracting the dye by incubation with 4M guanidine-HCl (Sigma-Aldrich) overnight at room temperature. The extracted dye solution was diluted 10-fold and absorbance was measured at 490 nm Using spectrophotometer (SpectraMax M5, USA). Cellular ALP activity was evaluated using a QuantiChrom™ Alkaline Phosphatase Assay Kit (BioAssay system #DALP-250) according to the manufacturer's instructions [21].

Adipogenic Differentiation

WJMSCs at Passage 3 were harvested, counted, and seeded at a concentration of 10×10^4 per well into 6 well plate. The cells were divided into two groups, the first group cultured in adipogenic differentiation media composed of [DMEM supplemented with 10% FBS, 1μM dexamethasone, 500 μM isobutylmethylxanthine (IBMX), 5μg/ml insulin and 200μM Indomethacin]. The second group was cultured in normal growth media and used as a control, with the media being changed twice per week for 2 weeks. The adipogenic differentiation capability was tested by Oil-red-O stain. The images were taken using an inverted light microscope. The staining was assessed quantitively by extracting the dye using isopropanol incubation for 15 minutes at room temperature, and absorbance of a two-fold dilution of the extracted dye was measured at 550 nm [21].

***In vivo* study**

The cells used for treatment were divided into two groups. For the first group, WJMSCs were treated with HA (Sigma Aldrich catalog number 53747) at a concentration of 1 mg/ml for 14 days and in the second group, the cells were maintained in normal growth media. The animal study was carried out using 72 male Sprague-Dawley rats weighing ~250-300 g and in accordance with the Guide for the Care and Use of Laboratory Animals approved by the ethical committee (ECSR), Zagazig University. The rats were divided randomly into 4 groups: (1) **Sham group** (n=18) involved rats undergoing an identical surgical procedure, but without renal pedicle occlusion **(2) Control group (IR injury) (n= 18)** involved the renal pedicles (artery and vein) being obstructed for a period of 45 minute to induce the ischemia reperfusion injury to create acute renal failure model **(3) WJMSCs group (n=18) was** the same as in IR injury group with administration of 1×10^6 MSCs and **(4) WJMSCs/HA groups (n=18)** was the same as the IR injury group with administration of 1×10^6 MSCs pretreated with HA. The treatment groups included MSCs and MSCs/HA group, in which the cells were injected directly into the cortical region of the left kidney using 24-gauge syringe in 2-3 injections of 0.03-0.05 ml each at different locations along the lateral aspect of the kidney. Animals were sacrificed at 1,4 and 7 days after surgery and blood, urine, and tissue samples were collected to assess the efficiency of the treatment.

Kidney Function assessment

Blood and urine samples were collected at the sacrifice time of all animal groups, the blood was centrifuged and serum was collected. Urine samples were collected using metabolic cage biochemical parameters, including creatinine, blood urea nitrogen (BUN) and creatinine clearance were measured by standard laboratory methods. The anti-inflammatory marker monocyte chemoattractant protein 1 (MCP-1) was measured in the serum of all groups at day 7 post-surgery using MCP-1 Rat ELISA Kit (Abcam, ab100778) according to the manufacturer's protocol. Anti-oxidant superoxide dismutase (SOD) activity was evaluated in all groups at day 7 post-surgery using Superoxide Dismutase Colorimetric Activity Kit (Invitrogen, EIASODC) according to the manufacturer's protocol. The degree of fibrosis was evaluated in the tissue sample of all experimental animals 7 days post-surgery through measuring the total collagen content using Total Collagen Assay Kit (Biovision, K218).

Gene Expression

Total RNA was extracted from kidney tissue of sham, MSCs and MSCs/HA groups using RNeasy Mini Kit (Qiagen,74104). Isolated RNA was purified using RNeasy MinElute Cleanup Kit (Qiagen,74204). For cDNA synthesis, 1 μg RNA was transcribed using QuantiTect Reverse Transcription Kit (Qiagen, 205310) according to the manufacturer's protocol. Kidney-specific metanephric differentiation marker Cadherin 11 and CD 24 mRNA expression was analyzed using 2 μl of the obtained cDNA using Real-Time PCR system (Applied Biosystems, USA). Primer sequence used for Cadherin11 and CD24 are summarized below in table 1.

Table 1. Primer sequence used for Cadherin11 and

Gene	Sense	Primer sequence
Cadherin 11	Forward	5′-ATCGTCATTCTCCTGGGTTG-3′
	Reverse	5′-GCCACCACATAGAGGAAAGG-3′
CD 24	Forward	5′-GCCAGTCTCTTCGTGGTCTC-3′
	Reverse	5′-TGTTTTTCCTTGCCACATTG-3′
GAPDH	Forward	5′-CCTGCACCACCAACTGCTTA-3′
	Reverse	5′-GGCCATCCACAGTCTTCTGAG-3′

The reactions were initially heated for 10 min at 95°C, followed by 40 cycles of 15 seconds at 95°C and 60 seconds at 60°C were performed. After a final denaturation (melt curve stage) step of 1 min at 95°C, the amplification curve was recorded. Cadherin 11 and CD 24 mRNA was quantified in proportion to GAPDH as endogenous gene. The expression levels were scaled relative to the sample with the lowest expression level (Sham group).

Histological analysis

The kidney tissues were collected at day 7 post-surgery then cut into two equal halves, one half was fixed in 10% neutral buffered formalin and processed for paraffin blocks and the other half was kept in liquid nitrogen for RT–PCR analysis. Paraffin tissue blocks were cut into 5µm thickness sections and stained with hematoxylins & eosin stain (H&E), images were taken using a light microscope (Zeiss Axiovert, Germany). 10 fields were examined for cortex and medulla region by high power field. Degeneration and regeneration score were examined as described by Kinomura *et al*. [22]. In brief, the degree of tubular injury was quantified as a score between 0 and 5 as the following: score (0) for normal tissue; score (1) indicate that less than 20% of the tubules exhibiting tubular basement membrane injury, swelling, vacuolar degeneration and necrosis; score (2) involve 20-40% tubules injury, score (3) for 40-60%, score (4) 60-80% and score (5) for more than 80% of injured tubules.

Statistical analysis

Data were analyzed with student's *t*-test or one-way ANOVA using GraphPad Prism software version 7.04 (GraphPad Software, Inc., La Jolla, CA). $P < 0.05$ was considered statistically significant.

3. Results

3.1 Isolation and Characterization of WJMSCs

3.1.1. Cell Growth and expansion

Mesenchymal stem cells were isolated enzymatically from Wharton's jelly tissue of umbilical cord and

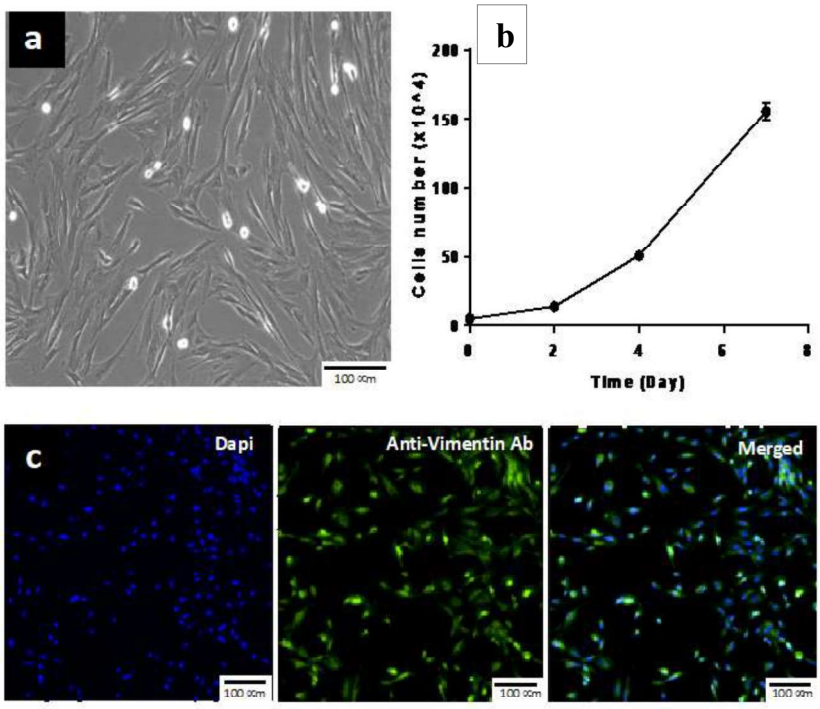

Fig. 1. Isolation and characterization of MSCs from Wharton's jelly tissue. (a) Morphology of WJMSCs at passage 3, (b) growth curve of WJMSCs during *in vitro* cultures (c) immunofluorescent staining for mesenchymal marker vimentin

demonstrated spindle-shaped morphology after 7 days of culture. The cells displayed a more fibroblast-like shape with increasing passage number, and at passage 3 the cells were able to form homogenously fibroblastic cell monolayers (Figure 1a). WJMSCs also possess high proliferation rate and cell growth kinetic (Figure 1b). WJMSCs showed short PDT value of 30±0.34 hours. The colony forming unit fibroblast (CFU-F) used to evaluate the ability of WJMSCs to proliferate and form colonies revealed the presence of cologenic cell population with a value of 14±0.58.

Immunofluorescence staining

Immunocytochemical detection of mesenchymal marker vimentin on WJMSCs showed positive cytoplasmic staining for MSCs markers indicating that WJMSCs possess MSCs features. The cytoplasmic marker vimentin stained with green, nuclei were counterstained with DAPI (blue) (Figure 1c).

Differentiation potential of WJMSCs

The differentiation potential of WJMSCs toward the osteogenic and adipogenic lineages was confirmed by incubating the cells with osteogenic and adipogenic differentiation medium respectively. The cells cultured in osteogenic differentiation medium showed calcium formation, which was detected by Alizarin red staining (Figure 2a). The optical density of the extracted dye showed a value of 0.39±0.03 compared to 0.04 for the control, while no calcium was detected in the control groups (Figure 2d). Additionally, alkaline phosphatase activity in osteogenic differentiated cells was significantly higher compared to the control group, (Figure 2c). Meanwhile, the cells cultured in adipogenic differentiation medium showed accumulation of lipid droplets which was detected by Oil red O stain (Figure 2b), and the spectrophotometric analysis of the extracted dye revealed that the differentiated cells have a value of 0.12±0.01compared to 0.02±0.01for the control groups, in which no lipid vacuoles were observed.

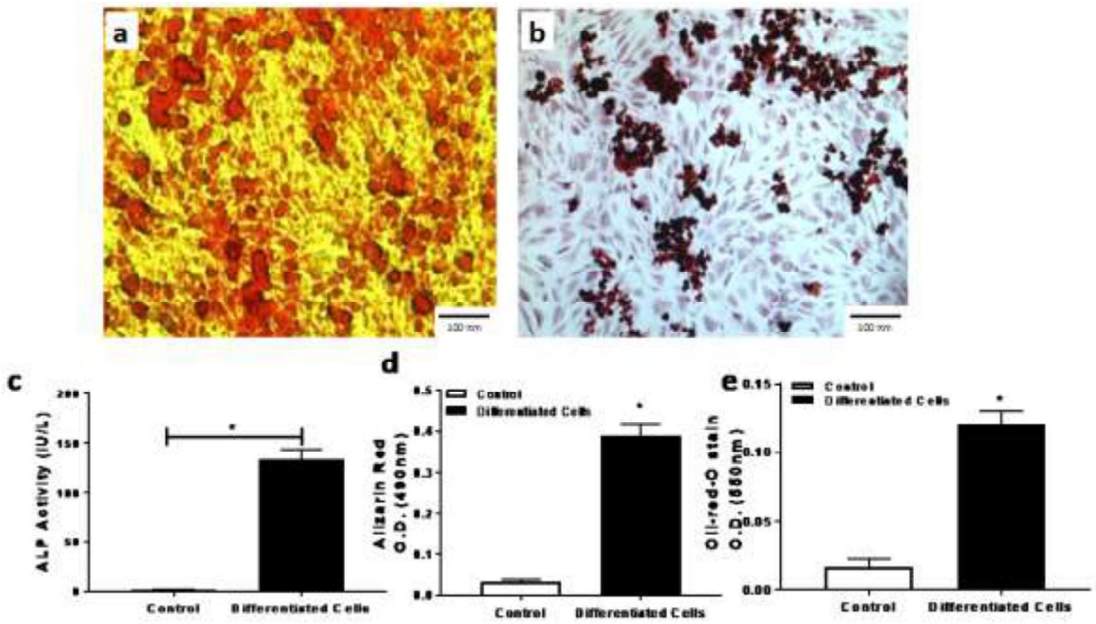

Fig. 2. Differentiation Capability of WJMSCs, (a, c and d) osteogenic differentiation capability of WJMSCs, (b,e) Adipogenic differentiation (n=3, *P<0.05)

***In vivo* study**

Analysis of biochemical marker to evaluate Kidney function

Renal function was assessed in all experimental groups by measuring the biochemical parameter BUN, Serum creatinine and creatinine clearance at days 1, 4 and 7 post-surgery. The obtained data revealed that the renal function returned to its normal level at day 7 post-surgery in all groups, even though rapid recovery happened in both treatment groups (MSCs and MSCs/HA) compared to the positive control (IR) group. MSCs preconditioned with HA help in shortening the recovery time compared to MSCs group only.

Serum creatinine and BUN level (mg/dl) at day 1 decreased in both treatment groups compared to IR group, while MSCs/HA showed significantly lower value compared to IR group ($p<0.05$). At day 4 both treatment groups showed that BUN and creatine level were decreased compared to IR group, meanwhile, the treatment groups showed that creatinine and BUN level at day 4 were significantly decreased compared to the same

groups at day 1 ($p<0.05$). At day 7 BUN and creatinine level returned to their normal values in all groups (Figure 3A-B).

Creatinine clearance value (ml/min) of the treatment groups was statistically significantly higher than that of IR group at all time points. Meanwhile, MSCs/HA showed significant higher values compared to IR group ($p<0.05$) (Figure 3C).

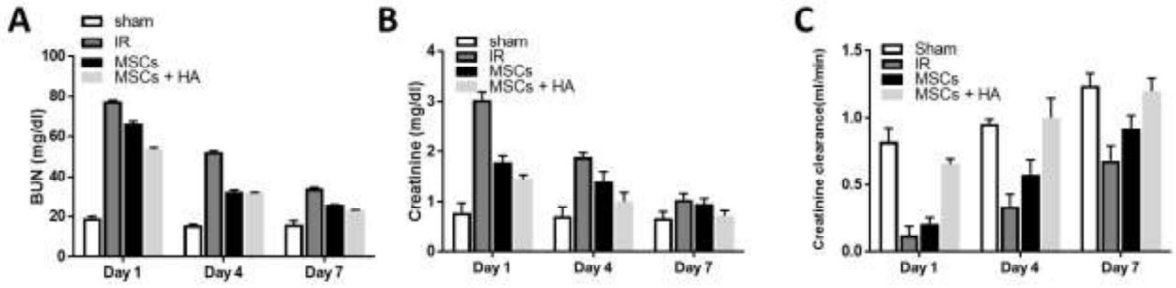

Fig. 3. Biochemical evaluation of kidney function at 1, 4 and 7 days in all experimental groups. (A) Blood Urea Nitrogen level (mg/dl), (B) Serum Creatinine level (c) Creatinine Clearance (ml/min.) (n=6, *P<0.05)

The antioxidant and anti-inflammatory effects of MSCs were evaluated at day 7 post-surgery in all experimental groups by measuring the activity of Super oxide dismutase (SOD) and monocyte chemoattractant protein 1 (MCP-1) concentration respectively. The anti-inflammatory marker MCP-1 values (pg/ml) for both treatment groups was decreased compared to IR group, moreover the MCP-1 level of MSCs/HA group significantly decreased compared to IR group ($p< 0.05$) (Figure 3A). The antioxidant activity of SOD was higher in the treatment groups compared to IR group. Meanwhile, the SOD activity increased significantly in MSCs/HA group increased compared to IR group ($p<0.05$) (Figure 3B).

Total collagen deposition in renal tissue was assessed among all experimental groups at 7 days post-surgery. The collagen content decreased significantly in the treatment groups compared to IR group, while the decrease was significant in MSCs/HA group in comparison to IR group ($p<0.05$). (Figure 3C).

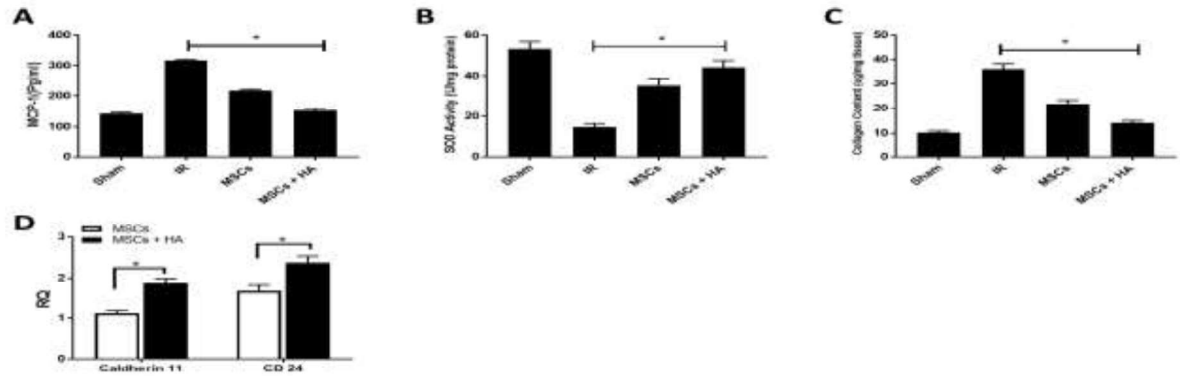

Fig. 4. The effects of MSCs and MSCs/HA treatment on (A) the anti-inflammatory marker MCP-1 values (pg/ml), (B) The antioxidant activity of SOD Antioxidant, (C) Fibrosis level (ug/mg tissue) in all experimental groups at day 7 of surgery (n=6, *P<0.05)

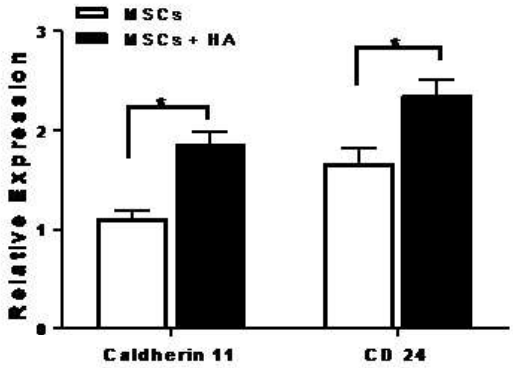

Fig. 5. The expression levels of metanephric markers Cadherin 11 and CD 24 in the treatment group (n=3, *P<0.05)

Gene Expression

The expression levels of metanephric markers Cadherin 11 and CD 24 was significantly higher in MSCs/HA group compared MSCs (P< 0.05), the data was normalized to sham group (Figure 4) and presented for the treatment group (Figure 5).

Histological Study of the Kidney

To examine the effect of WJMSCs on the treatment of renal injury, histomorphological examination was performed by H&E staining and the degree of injury was calculated among the experimental groups. The results indicated that the renal injury score increased in all

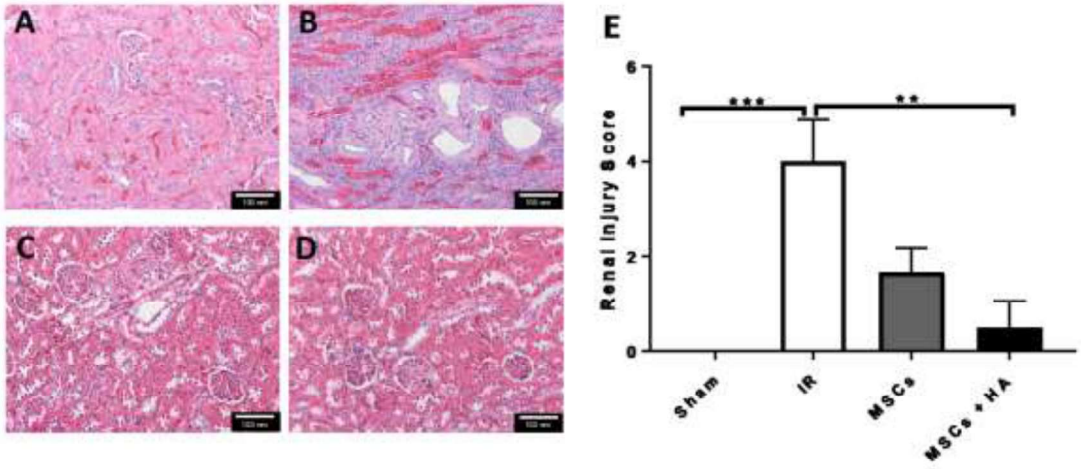

Fig. 6. Histological analysis of Kidney specimens at day 7 showing (A) normal kidney structure of sham group, (B) IR group, (C) MSCs group, (D) MSCs / HA group. scale bare: 50 µm, (E) Degree of renal injury.

groups compared to the sham group, the highest score was observed in IR group. meanwhile, the renal injury score of MSCs/HA was significantly decreased compared to IR group (Figure 6).

Discussion

Kidney diseases, including acute and chronic diseases, are still a challenging health problem for patients all over the world. Since these diseases eventually induce renal failure, the patients with end stage renal diseases is increasing annually. Stem cell therapies offer a promising option for kidney failure treatment due to their ability to differentiate into multiple cell lineages, in addition to their ability to decrease the inflammation and oxidative stress in injured tissue. In this study, MSCs were isolated from Wharton's jelly tissue and expanded invitro. Wharton's jelly tissue is considered an important alternative source for MSCs because it utilizes unused tissue to get viable cells. The isolated cells showed high cell viability and proliferation; moreover, these cells were able to exhibit MSCs feature such as expression of mesenchyme marker, ability to differentiate into multiple cell type (such as osteocyte and adipocyte), and the ability to modulate the immune response during allogenic transplantation. To assess the ability of stem cells to treat kidney diseases, an acute kidney injury model was established by IR injury. Due to the fact that IR injury causes significant increase in serum creatinine and BUN with significant reduction in creatinine clearance, the clinical parameter was confirmed by histological examination, which showed increase in the renal tubular injury in positive control group. These finding agrees with previous studies [23-25].

Renal function returned to its normal level at day 7 post-surgery in all groups, even though faster recovery occurred in both treatment groups (MSCs and MSCs/HA) compared to the positive control group. Histological examination of kidney tissue displayed minimal tubular and interstitial damage with signs of regeneration in the treatment groups. These findings corroborate previous studies that demonstrate the efficacy of stem cell in renal failure treatment [26-32]. Additionally,

MSCs preconditioned with HA demonstrated faster renal function recovery than non-treated MSCs, thus the use of HA along with MSCs increase the efficacy of treatment by enhancing the cell proliferation and recruitment in the injured tissue, regulation of cell–cell interaction and cell-matrix adhesion these finding agreed the previous studies demonstrated that HA enhance the stem cell therapy. [33,34].

Although the mechanism of tissue repair by stem cells is not well understood, our result suggests that some cells engrafted into the injured tissue start to differentiate into metanephric mesenchyme, while other cells provide renoprotection through secretion of some paracrine factors with regenerative, anti-apoptotic, antioxidant and anti-inflammatory effect. These finding were in accordance with previous studies [35-39].

Conclusions

This study evaluates the improvement of renal function of acute kidney injury model induced by IR using MSCs derived from Wharton's jelly tissue. WJMSCs offer alternative source for adult MSCs able to improve the renal function. Our results suggested that WJMSCs were able to enhance tissue repair by promote the differentiation of MSCs into metanephric mesenchyme and provide renoprotection by reducing the inflammation and oxidative stress resulted from IR injury. Utilizing MSCs along with hyaluronic acid enhance the ability of WJMSCs to repair kidney tissue injury. Further studies are required to address the underlying mechanism behind the effect of HA on MSCs.

Conflict of interest statement. None declared.

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Original article

Sociodemographic Determinants of Kidney Disease in Egyptian Tertiary Health Center

Ahmed Yamany Ali[1] ,Sahier Omar Elkhashab[2] and Mohammed Mohamed Abdel Razik[3]

[1]Lecturer of Internal Medicine, [2]Assistant Professor of Internal Medicine, [3]Lecturer of Community, Cairo University, Egypt

Abstract

Introduction. Chronic kidney disease (CKD) is increasingly recognized as a public health problem, and is linked to the risk of development of cardiovascular disease (CVD) with their accompanying morbidity, mortality and increased healthcare costs. The study aims to outline a planned control strategy for renal diseases.

Methods. This study was conducted among CKD Egyptian patients (n=556) in the nephrology outpatient clinic of Kasr Al Ainy hospital. Personal and family socio-demographic characteristics, present history, habitual drug intake, family history of kidney diseases, laboratory findings and pattern of care in the outpatient clinic were obtained.

Results. Among the participants, diabetes mellitus (DM) and hypertension were the most common causes of CKD (56% and 40%) respectively. Older age and male sex are associated with low estimated glomerular filtration rate (eGER) (P <0.001). Patients with middle and high sociodemographic status were significantly associated with higher eGFR than those with low sociodemographic status (P <0.001).

Conclusions. Old age, female gender, illiteracy and low sociodemographic status were significantly associated with low eGFR. On the other hand, smoking, habitual intake of analgesics, residential exposure to chemicals, family history of CKD and lack of compliance for regular follow up were not significantly associated with low eGFR in Egyptian CKD patients.

Key words: chronic kidney disease-diabetes mellitus-illiteracy-morbidity-socio-demographic status

Introduction

Chronic kidney disease (CKD) is one of the most widespread non-communicable disease (NCD). CKD is consistently associated with enormous medical, social, and financial burdens for individuals, their families, and national health systems [1]

CKD definition encompasses all grades of reduced renal function associated with poor outcomes, repeated hospitalization, and increased risk of morbidities as anemia and cardiovascular complication and mortality [2].

The epidemiological pattern of chronic kidney disease widely differs among the societies, however it is not well established due to the lack of national renal registries and sufficient representing data specifically in developing countries and eventually in Egypt [3].

CKD prevalence in US escalates with age (4% at age 29-39 y; 47% at age >70 y), more in blacks [4] while in the Australian AusDiab kidney study, the prevalence of impaired GFR was 11.2% and increased with aging (from 0.01% in the 25 to 44 y age group to 54.8% in patients with age >65 y) [5].

The Fogarty International Center (FIC) of U.S. has reported that the global burden of renal disease confers to ~830 000 demises per year and 18 867 000 disability-adjusted life years (DALY) [6] and this rank of high mortality and disability is similar across World Bank regions, particularly East Asian and Pacific regions [7].

Aside the well-recognized etiological factors of developing CKD such as diabetes, hypertension and glomerular disorders, there are the socio-demographic aspects (age, sex, education and occupation), thus assessing these aspects are of the utmost importance.

No adequate data on the different clinical patterns of renal disorders in Egyptian populations are present owing to the scarcity of research, sparsity of renal regional registries, medical records and filing systems inadequacy. An Egyptian study has concluded that CKD and acute kidney injury were the dominant causes of hospital admission. Sepsis, hyperkalemia, and HTN are common risk factors of mortality in Egyptian patients with kidney disease [8].

The aim of the study was to outline the sociodemographic profile, highlighting the various pattern of renal diseases among attendants to outpatient clinics of Kasr Al Ainy hospital and to determine the potential risk factors and related outcomes for planned control strategy.

Correspondence to: Ahmed Yamany Ali, Lecturer of Internal Medicine, Cairo University, Egypt, Madina monoura street, ard ellawaa, Giza, Egypt; Phone: +0201110006233; Fax: +20 26 28 884; E-mail: HYPERLINK "mailto:themythaysa@kasralainy.edu.eg"themythaysa@eg.edu.alainykasr