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Modulation of Nephrotoxicity Induced by Gentamicin with Bone Marrow Mesenchymal Stem Cells and *Moringa Oleifera* Extract

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The study was undertaken to evaluate the protective effect of bone marrow mesenchymal stem cells (BM-MSCs) and *Moringa oleifera* extract (MOE) against gentamicin (GN)-induced nephrotoxicity in male albino rats. Thirty two adult male rats were divided into four groups including the control group, the group injected i.p with a single dose of GN (100 mg/kg b.w), the group treated orally with MOE (400 mg/kg b.w) for 6 days then injected with a single dose of GN and the group was injected with a single dose of BM-MSCs ($5x10^5$cells) by tail vein then injected with GN. At the end of experiment blood and kidney tissue samples were collected for estimation of different biochemical parameters. The results recorded a significant increase in BUN, serum KIM-1, cystatin C, creatinine, sodium and renal MDA accompanied with a significant decrease in serum calcium, renal GSH, SOD and CAT in GN alone-treated group as compared to control group. Co administration of MOE or BM-MSCs before GN injection improved all above parameters when compared with GN administered group. It could be concluded that MOE and BM-MSCs have a therapeutic and protective action against AKI induced by GN administration which manifested by lowering kidney markers and MDA contents and elevation in antioxidant profile.

Keywords: Gentamycin, Nephrotoxicity, Bone marrow mesenchymal stem cells, Moringa oleifera

Introduction

The kidneys, the major control system maintaining homeostasis of body and a central detoxification organ, are the major targets for the toxic effects of various chemical agents and drug exposure. Thus drug-induced acute kidney injury (AKI) is a frequent entity in clinical medicine. The incidence of nephrotoxic or AKI is difficult to estimate due to the variability of patient populations and the criteria of AKI. However, nephrotoxicity has been reported to contribute to 8-60% of hospital acquired AKI cases [1].

The aminoglycoside gentamicin (GN) is widely antibiotic used in the treatment of infection caused by gram negative bacteria [2]. It was defined to possess significant nephrotoxic action in man and experimental animals [3] due to its accumulation in proximal renal tubules which in turn leads to brush border network damage [4]. The nephrotoxicity involves renal free radical production and accumulation, which had been suggested as a causative agent of cell death in different pathological states including various models of renal diseases [5] such as consumption of antioxidant defense mechanisms, glomerular

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congestion and acute tubular necrosis [6], leading to diminished creatinine clearance and renal dysfunction.

Nephrotoxicity is traditionally diagnosed using serum markers blood urea nitrogen (BUN) and creatinine levels which get elevated only after significant (approximately 30%) kidney damage [7]. They are also influenced by age, gender, muscle mass, muscle metabolism, diet, medications, and hydration status [8]. As these markers are insensitive and lack specificity, recently, novel early biomarkers have been suggested to evaluate early kidney damage both in preclinical species and human. Kidney injury molecule-1 (KIM-1) is among the most promising ones. KIM-1 is expressed on the surface of tubular epithelial cells in the kidney. KIM-1 levels are undetectable in normal kidneys, whereas elevated KIM-1 expression was detected in the ischemic kidney in the animal model of disease [9], as well as in humans [10]. KIM-1 could be utilized as a nephrotoxicity biomarker in preclinical studies of drug candidates [11]. The Food and Drug Administration (FDA) and European Medicines Agency (EMA) had recently recognized KIM-1 as an appropriate biomarker for renal injury in preclinical studies of pharmacologic agents [12]. Another sensitive biomarker in detecting site specific nephrotoxicity is Cystatin C (CysC) which is a small molecule of 13.3 kDa, 122 amino acid non-glycosylated basic cysteine protease (lysosomal proteinases) inhibitor, preventing breakdown of certain intracellular and extracellular proteins within the body, constitutively expressed by all nucleated cells, and is synthesized and secreted to the plasma at a steady rate [13]. Serum CysC was used as glomerular filtration rate (GFR) marker in toxicology studies although it has been widely used in clinic [14].

Stem cell-based therapy has a great attention in treatment of complex disorders such as AKI. It holds a great promise for the repair of injured tissues and organs, including the kidney [15] and constitute a promising resource in regenerative medicine for the generation of appropriate cell types in cell replacement therapy [16]. Many studies suggested that mesenchymal stem cells (MSCs) possess potential in the treatment of AKI [17,18]. Among the different types of stem cells bone marrow-derived mesenchymal stem cells (BM-MSCs), also known as marrow stromal cells [19] or mesenchymal progenitor cells [20], are defined as self-renewable, multipotent progenitor cells with the capacity to differentiate into several distinct mesenchymal lineages [21]. BM-MSCs are regarded as an attractive therapy for renal tissue regeneration, as the cells can be isolated from the bone marrow of patients and be modified in vitro by vector-mediated gene delivery easily, and they also avoid the ethical ambiguities of using embryonic stem cells [22].

Recently, great attention has been focused on traditional and herbal medicine for the treatment of renal disease. *Moringa oleifera* (MO) has rich antioxidant content and diverse therapeutic properties. The different parts of MO are reported to possess various pharmacological actions and nutritional qualities [23]. MO has a potent antioxidant and free radical scavenging activities in vitro and in vivo [24,25]. It was also reported that MO has protective action to prevent the renal damage induced by diabetes through its protective effect on the oxidative status and inflammatory cytokines in the kidneys of diabetic rats [26]. The present study was carried out to evaluate the protective effects of MO extract and BM-MSCs against GN-induced renal toxicity in rats.

Material and Methods

Chemicals and kits

Gentamycin sulphate (GN) and aqueous-ethanolic Moringa Olifera extract (MOE) were purchased from Sigma Chemical Co. (St. Louis, Mo, USA) and Mepaco Arabian Pharmaceutical co., (Cairo, Egypt), respectively. Kits for creatinine, blood urea nitrogen (BUN), Kidney Injury Molecule-1 (KIM-1), lipid peroxidase (MDA), reduced glutathione (GSH), catalase (CAT), superoxide dismutase (SOD) and ELISA kits of Cystatin C were purchased from Bio Diagnostic (Cairo, Egypt).

Experimental animal

Male albino rats (weighing, 140 -160 g) were purchased from animal house colony, Biochemical laboratory, Faculty of Medicine, Cairo University. The animals were housed under standard conditions with a 12 hr light/12 hr dark cycle and thermally controlled (25 ±1 OC). Water and food were provided *ad libitum*. All animals were received humane care in compliance with the guidelines of the Animal Care and Use Committee of Faculty of Medicine, Cairo University and the National Institute of Health (NIH publication 86-23 revised 1985).

Preparation of bone marrow- derived Mesenchymal Stem Cells (BM-MSCs)

Isolation of rat BM- derived MSCs

MSCs were collected from three-months old male albino rats (140 -160 gm). Briefly, the rats were euthanized by cervical dislocation and their tibias and femurs were cleared of muscle and connective tissue. Bone marrow cells were aspirated using an 18-gauge needle with phosphate-buffered saline (PBS) and passed through 70 µm nylon gauze. The cells were washed twice for 5 min each by centrifugation at 150 x g and re-suspended in Dulbecco's modified Eagle's medium (DMEM; GIBCO / BRL) supplemented with 10% fetal bovine serum (GIBCO /BRL). Nucleated cells were isolated with a density gradient [Ficoll/Paque (Pharmacia)] and re-suspended in complete culture medium supplemented with 1% penicillin/streptomycin (GIBCO/BRL). Cells were incubated at 37°C in 5% humidified CO2 for 12-14 days as primary culture. Media was changed every 2-3 days. When large colonies developed (80-90% confluence), cultures were washed twice with phosphate buffer saline (PBS) and the cells were trypsinized with 0.25% trypsin in 1mM EDTA (GIBCO /BRL) for 5 min at 37°C. After centrifugation, cells were re-suspended with serum-supplemented medium and incubated in 50 cm3 culture flasks (Falcon). The resulting cultures were referred to as first passage cultures [27]. On day 14, the adherent colonies of cells were trypsinized and counted.

Phenotypic analysis of BM-MSCs

Flow cytometric analysis for MSC phenotype was doing using FC500 (Beckmann). Cells were harvested and washed in flow cytometry buffer and incubated for 20 min in flow cytometry buffer containing fluorescein-conjugated monoclonal antibodies directed against differentiation of MSC antigens (CD29, CD49d, CD105, Chemicon) and against hematopoetic antigens (CD34 and CD45, Miltenyl Biotech). Cells at passages 3-5 were used for in in vivo experiments.

Experimental design

After one week of an acclimatization period, the rats were divided into four groups (8 rats/group) and treated daily for a period of 6 successive days as follow: group 1; Vehicle control group received an intraperitoneal (i.p.) injection of 0.5 ml of normal saline, group 2; rats injected i.p with a single dose of 100 mg/kg b.w GN according to Sonkar et al. [28], group 3; rat treated with a daily oral dose of MOE (400 mg/kg b.w) for 6 days then i.p. injected with a single dose of GN [29], group 4; rats received a single injection of BM-MSCs ($5x10^5$ cells) [30] then injected with a single dose of GN. Animals were left for 24 h after the last injection then blood samples were collected via the retro-orbital venous plexus under diethyl ether anesthesia. Sera were separated using cooling centrifugation and stored at -20 ^{O}C until analysis. The serum samples were used for the determination of creatinine, blood urea nitrogen (BUN), kidney injury molecule-1 (KIM-1) and Cystatin C. levels according to the manufacturer's instructions. After the collection of blood samples, all animals were sacrificed and sample of kidney from each rat was dissected, weighed and homogenized in phosphate buffer (pH 7.4) to give 20% w/v homogenate and was used for the determination of MDA then it was further diluted to give 2% and 0.5% dilution for the determination of GSH (2%), CAT and SOD (0.5%) activities [31].

Statistical analysis

Data were represented as mean ± SD of different groups. One-way analysis of variance (ANOVA) followed by Tukey's post-hoc test was used to compare between the groups for parametric data. For non-parametric data, Kruskal-Wallis test was used to compare between the groups. The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows.

Results

The results of the current study revealed that single i.p. injection of GN at dose of 100 mg/kg b.w. increased the levels of serum BUN, creatinine, KIM-1 and cystatin-C compared to control group. The pretreatment with MOE or BM-MSC induced a significant improvement of the levels of all parameters tested compared to GN alone treated group. However the recorded values were still higher than the control group. The recorded improvement in both groups was more pronounced in the group treated with BM-MSC (Table 1).

The effect of MOE and BM-MSC on oxidant/ antioxidant in rats treated with GN (Table 2) showed that GN induced a significant increase in MDA in the kidney tissue accompanied with a significant decrease in SOD, CAT and GSH compared to the control group. Pretreatment with MOE for 6 days or a single dose of BM-MSC could induced a significant decrease the elevation of MDA and also induced a significant increase in the reduction of SOD, CAT and GSH resulted from GN. Although the co-treatment with MOE or BM-

MSC plus GN induced a significant improvement in the antioxidant status, these parameters were not normalized and still differing than the control group.

The results illustrated in Fig. 1 and 2 indicated that injection with a single dose of GN resulted in a significant increase in Na+ level accompanied by a significant decrease in Ca^{++} level compared to control. Treatment with MOE or BM-MSC before GN alleviated the alteration in both electrolytes levels.

Discussion

The nephrotoxicity of aminoglycoside GN is well documented. All rats injected with a single dose of GN (100 mg/kg b.w) showed nephrotoxic effects. In agreement with previous studies which exhibited that administration of GN induced nephrotoxicity in various experimental animal models including mice, rat and rabbit [32-34].

In the current study the levels of BUN and serum creatinine were significantly higher in GN treated group than the control. These findings were consistent with data obtained by other researchers [35,36]. Additionally, nephrotoxicity induced by GN was confirmed by marked elevations in serum KIM-1 and Cystatin-C concentrations when compared with the control group. This finding is in agreement with a recent report [36]. Elevation in serum parameters in GN-treated rats was probably the result of tubular necrosis with a consequent decrease in the number of functioning nephrons [37].

TABLE 1. Effect of BM-MSCs and MOE on serum parameters of kidney injury of rats treated with GN

Parameter / Groups	BUN (mg/dL)	Creatinine (mg /dL)	KIM-1 (ng/mL)	Cystatin-C (ng/mL)
Control	42.8 ± 13.3^{a}	0.15 ± 0.06^{a}	3.1 ±1.0^{a}	5.4 ±1.0^{a}
GN	90.2 ± 19.6^{b}	1.61 ± 0.55^{b}	13.2 ±4.3^{b}	22.0 ± 8.9^{b}
MOE then GN	87.5 ± 10.7^{b}	0.64 ± 0.12^{c}	6.1 ±1.7^{c}	13.6 ±3.6^{c}
BM-MSCs then GN	67.3 ± 8.4^{c}	0.39 ± 0.12^{d}	5.7 ±1.7^{c}	9.8 ±3.8^{d}

BUN: Blood Urea Nitrogen, KIM-1 and Cystatin-C, data is expressed as Mean ± SD
Within each column, means superscript with different letters (a, b, c…..) are significantly different (P≤0.05)

TABLE 2. Effect of BM-MSCs and MOE on MDA and antioxidant capacity in the kidney tissue of rats treated with GN

Parameter / Groups	MDA (nmol/g tissue)	SOD (U/g tissue)	CAT (U/g tissue)	GSH (nmol/g tissue)
Control	1.3 ± 0.4^{a}	4.0 ± 1.0^{a}	147.6 ± 23.0^{a}	68.7 ± 8.2^{a}
GN	24.3 ± 7.4^{b}	0.6 ± 0.3^{b}	65.4 ± 22.6^{b}	24.9 ± 5.0^{b}
MOE then GN	12.7 ± 3.1^{c}	1.6 ± 0.5^{c}	116.1 ± 11.0^{c}	41.6 ± 5.4^{c}
BM-MSCs then GN	7.2 ± 2.3^{d}	2.2 ± 0.8^{c}	119.1 ± 14.0^{c}	50.9 ± 8.6^{d}

MDA: Malondialdehyde, SOD: Superoxide dismutase, CAT: catalase and GSH: Glutathione. Data is expressed as Mean ± SD
Within each column, means superscript with different letters (a, b, c…..) are significantly different (P≤0.05)

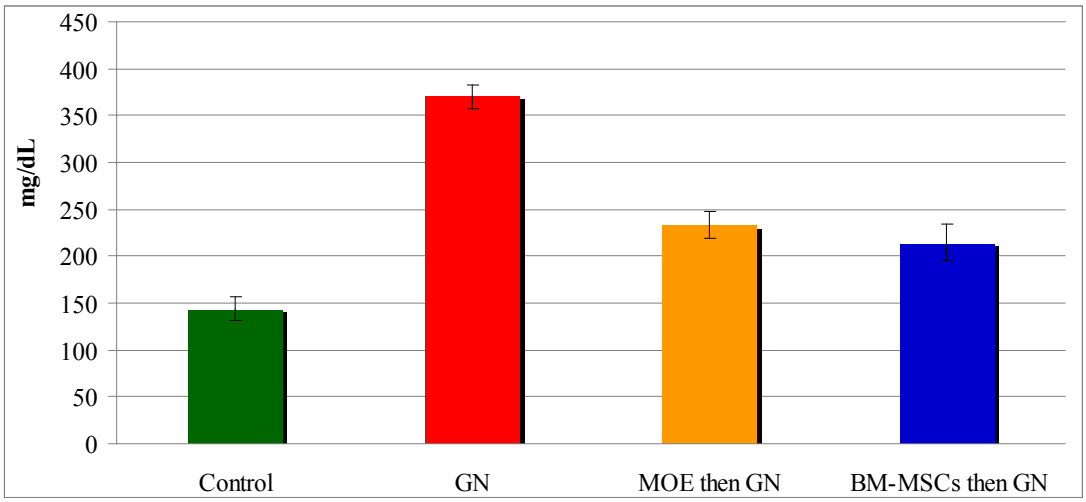

Fig. 1. Effect of BM-MSCs and MOE on serum level of sodium in rats treated with GN

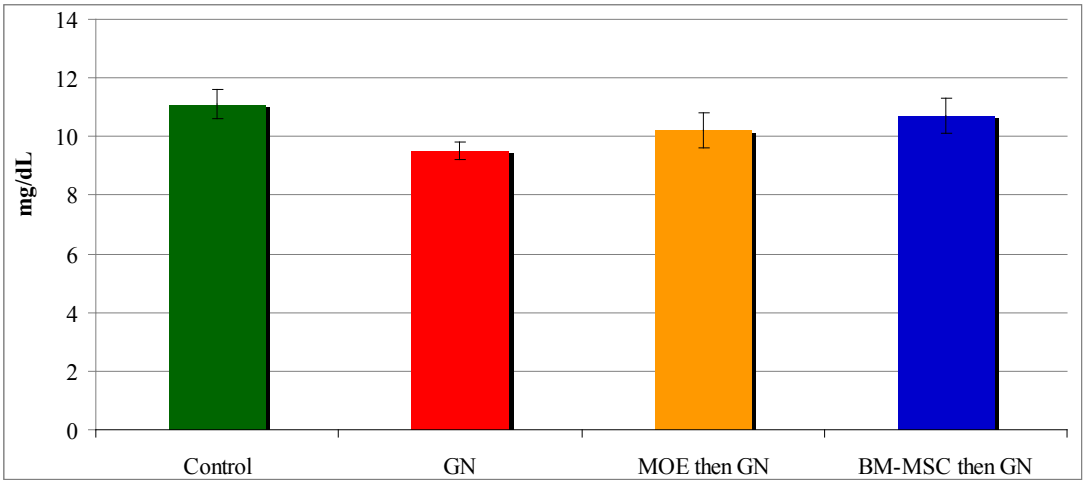

Fig. 2. Effect of BM-MSCs and MOE on serum level of calcium in rats treated with GN

Oxidative stress is one of the major features of GN-induced renal damage. The present work showed that GN injection altered various biochemical indicators of oxidative stress in kidney tissue. The level of renal lipid peroxidation (MDA) was increased whereas GSH content, CAT and SOD activities were decreased in GN-treated group when compared with the control. These results were in accordance with previous studies [38,39]. Several reports have been recognized that GN enhances the generation of reactive oxygen species (ROS). ROS may damage some macromolecules to induce cellular membrane integrity and necrosis via several mechanisms including peroxidation of membrane lipids, protein denaturation and DNA damage [5,40].

Lipid peroxidation alters the kidney functions via a proximal event in the injury cascade of GN nephrotoxicity. Some reports showed that GN acts as an iron chelator, and the complex of iron-GN is consider a potent catalyst of free radical production [41,42]. Additionally, GSH is a vital and most abundant cellular detoxifying antioxidant in the body. GN was reported to induce excessive production of hydroxyl radicals, superoxide anions and hydrogen peroxides and reactive nitrogen species in the renal cortex [38], resulting in the decrease of GSH levels due to its increased utilization in protecting \SH group containing proteins from free radicals. Similarly, decreased activities of SOD and CAT may be attributed to excessive formation of superoxide anions and hydrogen peroxide and/or their inactivation by excessive GN induced oxidants [39].

Kidney diseases and intake of some antibiotics such as aminoglycosides cause electrolyte imbalance. The present study showed significant changes in the levels of both serum electrolytes Na+ and Ca+ after GN intoxication as compared with control. Renal failure with electrolyte disturbance is potentially serious and causes high morbidity and mortality. It was documented that a second less side-effect of GN therapy is a disturbance of electrolyte homeostasis [43]. The current finding is in harmony with the observations of [44,45]. These authors reported that a slightly increased level of sodium and decreased level of magnesium and potassium in GN-treated rats caused by alteration of tubular reabsorption and glomerular dysfunction [46]. Additionally, Padmini and Kumar [47] confirmed lower levels of serum sodium which indicates kidney inability to conserve sodium and chloride. Also, haemodilution was appeared due to the decrease of sodium value via excess of water intake and/or increase production of endogenous water [47].

The current study revealed that a hypocalcemia in GN treated group when compared with the corresponding values of control group. These results are in agreement with the findings of Zahid et al. [48] in rabbits. Moreover, derangements of renal functions were caused by aminoglycosides which manifested by its accumulation on brush border and basolateral membranes of proximal convoluted tubules [49]. Liamis et al. [50] suggested that megalin receptor which found at the apical membrane of the proximal convoluted tubules can binds and induces endocytosis of the aminoglycosides. Moreover, the plasma membrane of renal proximal tubular cells is the first site of the interaction of aminoglycosides and cells which cause the depression of the apical membrane transporter resulted in the loss of phospholipids and brush border membrane enzyme which is early occurring after the administration of aminoglycosides. Consequently, it decreased the transportation of electrolytes (Calcium and Potassium), organic bases, and reduces Na+-K+ATPase activity [51]. Additionally, hypercalcemia was also reported by Parsons et al. [52] which is mediated by the decrease in re-absorption of calcium in the early distal tubules.

Previous reports indicated that co-treatment with different antioxidants may prevent or attenuate kidney damage induced by GN [53]. So, it is important to search for non-toxic and effective medicinal plants with anti-oxidative activity [54]. MO was the plant of choice which has great antioxidant properties. Pretreatment with aqueous -ethanolic MOE at a dose of 400 mg/kg b.w alleviated the increased kidney biomarkers BUN and serum creatinine. These results are similar to those previously reported in GN-treated rabbits [55], Checken [56] and rats [57]. Additionally, co-administration of MOE before GN injection in present work improved the serum KIM-1 and Cystatin-C levels when compared with GN alone treated rats.

Co-administration of MOE attenuated nephrotoxicity induced by GN as evidenced by the decline in renal lipid peroxidation level accompanied with increasing GSH content, SOD and CAT activities. These results were coinciding

partially with the results obtained by Al Tayib and El Badwi [57] and Omodanisi et al. [26] in rats, Das et al. [58] in mice, Ouédraogo et al. [55] in rabbits, Arafat et al. [56] in chickens and El-Azab and El-Habashi [59] in laying hens. The protective effect exhibited by MOE could be due to its antioxidant potential by scavenging the free radicals. The antioxidant properties may be mediated through several mechanisms including (1) direct trapping of the free radicals, (2) metal chelation activity [60] or (3) through preserving structural integrity of cell membrane which was supported by the data published previously [61]. These authors suggested that MOE induced protective effects against chemical induced hepatonephrotoxicity due to its ability to induce phase II detoxification pathway via promoting reduced glutathione conjugation with toxic metabolites generated from CYP450 pathway [61]. Additionally, Sokunbi et al. [62] reported that the protective effect of MOE could be attributed to the ability to antagonize the enhancement of lipid peroxidation, consequently stabilize the integrity of the cellular membranes. All these observations illustrated that the phytochemical constituents in MOE could contribute to its antioxidant activity and, hence, nephroprotection [60].

Sodium is one of the important electrolytes responsible for the maintaining of normal cells and organs and it used for the determination of diseases status in the laboratory analysis. The current results showed a marked decrease in serum Na+ level in the group received the combined treatment of MOE plus GN when compared to GN alone treated group. These data are in agreement with the previous studies obtained in previous reports [63,64]. This effect may manifested by the hypotensive effect of MOE which attributes to the presence of active phytochemical compounds such as niazinin A, niazinin B, niazimicin and niazinin A + B [65].

Also, the present results exhibited a significant increase in serum Ca+ level in GN-treated group pretreated with MOE. This finding was in coincidence with the observation of Voemesse et al. [66], who recorded a highest concentration of calcium, magnesium and iron contents in birds fed with MO leaf meal during juvenile growth. Another suggestion was obtained by Dangi et al. [67] who showed the leaves of MO possess highly potent alkaloid salts, which are considered as possible calcium channel blocking activities. Additionally, MOE was reported to have great nutritional properties since it rich in calcium, magnesium and iron, various vitamins and essential amino acids [66].

Several studies have applied bone marrow derived mesenchymal stem cells (BM-MSCs) against AKI in animal models [68,69]. BM-MSCs are defined as multipotent progenitor cells which had a unique properties due its immunomodula¬tory ability and the potential for differentiation into mesenchymal lineage [70,71] and different types of renal cells [72,73]. The current study showed that nephro-protective activity of BM-MSCs against GN toxicity, manifested by decreasing BUN serum creatinine, KIM-1 and cystatin-C concentrations. Partially similar results were obtained by Selim et al. [74] who showed recovery in kidney functions manifested by a decline in serum creatinine, urea, KIM-1 of rats administrated BM-MSCs injection along with cisplatin. Also, Reis et al. [69] demonstrated that BM-MSCs have been reported to minimize renal damage induced by GN. Another study showed a nephro-protective effect in mice treated with BM-MSC which indicated by a decline in BUN level and urine albumin: creatinine ratio in albumin-overloaded mice which served as chronic kidney diseases models [75]. Similar nephro-protective effects were obtained by Morigi et al. [71] and Gatti et al. [76] who illustrated the nephro-protective activity of MSCs in ischemia-reperfusion injury-in cisplatin- and in glycerol-induced AKI through paracrine and endocrine mechanisms.

As mentioned earlier, oxidative stress is considered as a major mechanism among several suggestions proposed in GN-induced nephrotoxicity [44] and contributes to AKI through increased production of reactive oxygen species and/or lowering endogenous antioxidants system [77]. BM-MSCs had the ability to ameliorate oxidative stress and augment the antioxidant defense system [78,74] (Moustafa et al., 2016; Selim et al., 2019). The present study demonstrated that BM-MSCs injection along with GN decreased renal MDA level and increased GSH content, SOD and CAT activities. These results were coinciding with the observations obtained by Ali et al. [79] who confirmed that BM-MSCs improved the injury induced by hypoxia in brain of rats exposed to NaNO2 through the improvement of the enzymatic and non-enzymatic antioxidant system. This improvement

may be indicated by lowered MDA, GSSG levels and oxidized GSSG ratio, and increased GSH level and GSH/GSSG ratio and/or induction of growth factors, chemokines, and cytokine leading to tissue repair [80,81]. Similar results were obtained in ischemia/ reperfusion injury in the kidney [82,83]. Additionally, the present work showed an enhancement in serum electrolytes in rats administrated BM-MSCs injection along with GN. Similar result reported that BM-MSCs protect against hypocalcaemia in cisplatin treated rats [78].

Conclusions

The present data indicate that GN induced kidney injury as indicated by the elevation of serum BUN, creatinine, KIM-1 and Cystatin-C along with increased the level of MDA and the decreased GSH and SOD in the kidney tissue. GN also induced a disturbance in serum electrolytes such as Na^{+} and Ca^{++}. MOE and BM-MSCs could alleviate these effects and protect the kidney from GN-induced injury. Both agents are safe and may be considered as protective agents against kidney injury of different drugs or toxicants.

Conflict of Interest Statement

There is no conflict of interest in this study.

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تعديل السمية الكلوية التي يسببها عقار الجنتاميسين باستخدام الخلايا الجذعية الوسيطة لنخاع العظام ومستخلص المورينغا أوليفيرا

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أجريت الدراسة لتقييم التأثير الوقائي للخلايا الجذعية الوسيطة لنخاع العظام ومستخلص نبات المورينجا أوليفيرا ضد السمية الكلوية الناتجة عن عقار الجنتاميسين في ذكور الفئران البيضاء .استخدمت في هذه الدراسة عدد 32 من الفئران الذكور البالغين قسمت إلى أربع مجموعات شملت المجموعة الضابطة، المجموعة التي تم حقنها بجرعة واحدة يالبريتون بعقار الجنتاميسين 100) ملجم /كجم وزن جسم(، المجموعة المعاملة لمده 6 ايام عن طريق الفم بمستخلص نبات المورينجا 400) ملجم /كجم وزن جسم (ثم جرعة واحدة عن طريق البريتون من عقار الجنتاميسين والمجموعة المعامل بجرعة واحدة من الخلايا الجزعية .(5x105cells) في نهاية التجربة، تم جمع عينات الدم والكلى لتقدير الدلائل الكيميائية الحيوية المختلفة .سجلت النتائج زيادة كبيرة في BUNوKIM-1، cystatin C ، الكرياتينين، الصوديوم في السيرم صاحبه وياده في تأكسد الدهون بالكلية مع انخفاض معنوي في كالسيوم السيرم وجلوتاثيون والسوبر اوكسيد ديسماتيز والكتاليز في نسيج الكلى للفئران المعالجة بالحنتاميسين وحده بالمقارنة مع المجموعة الضابطة .أثبتت النتائج ان المعاملة بالخلايا الجذعية او مستخلص المورينجا مع الجنتاميسين أدت إلى حدوث تحسنا معنويا في كل القياسات محل الدراسة بالمقارنة بالمجموعة المعالجة بالجنتاميسين .نستنتج من هذه النتائج أن المعاملة بالخلايا الجذعية أو مستخلص المورينجا لهما تأثير علاجي ووقائي ضد التهاب تسمم الكلى الناتج عن تعاطي عقار الجنتاميسين من خلال خفض مؤشرات الكلية وتقليل تأكسد الدهون بالاضافة إلى زيادة مضادات الأكسدة في نسيج الكلية.