



Review

Regenerative pharmacology for the treatment of acute kidney injury: Skeletal muscle stem/progenitor cells for renal regeneration?



Egle Pavyde^a, Arvydas Usas^a, Romaldas Maciulaitis^{a,b,*}

^a Institute of Physiology and Pharmacology, Medical Academy, Lithuanian University of Health Sciences, LT-44307 Kaunas, Lithuania

^b Department of Nephrology, Medical Academy, Lithuanian University of Health Sciences, LT-50009 Kaunas, Lithuania

ARTICLE INFO

Article history:

Received 2 January 2016

Received in revised form 25 February 2016

Accepted 13 March 2016

Available online 18 March 2016

Keywords:

Regenerative pharmacology

Mesenchymal stem cells

Acute kidney injury

Muscle-derived stem progenitor cells

ABSTRACT

Regenerative pharmacology and advanced therapy medicinal products is a relatively new and challenging field in drug development. Acute kidney injury (AKI) is a common clinical condition in nephrology with increasing incidence and high mortality rate. During the last few decades, researchers have been eagerly trying to find novel therapeutic strategies for AKI treatment, including advanced pharmacological therapies using mesenchymal stem cells (MSCs). Several types of MSCs have been thoroughly investigated, including bone marrow, adipose derived and umbilical cord blood MSCs and shown promising results in kidney repair. Research has demonstrated, that MSCs exert their effect through reduction of apoptosis, increased production of growth factors, suppression of oxidative stress and inflammatory processes, promotion of renal tubular cell proliferation, as well as by migration and direct incorporation into the renal tissue. Skeletal muscle-derived stem/progenitor cells (MDSPCs) are mesenchymal stem cell lineage of multipotent cells, demonstrating long-term proliferation, high self-renewal capacities, and ability to enhance endogenous tissue repair. The capacity of MDSPCs to regenerate a variety of different tissues following acute injury or destructive tissue diseases have been demonstrated in preclinical and clinical studies. MDSPCs were also reported to promote endogenous tissue repair via paracrine pathway. Considering advantageous properties of MDSPCs, the administration of these cells might be considered as a potential strategy for the treatment of AKI. However, to date, the therapeutic effect of MDSPCs for renal regeneration has not been investigated. This review reflects the current development in AKI treatment using different types of MSCs and the pilot results of the experimental study in vivo using a novel type of stem cells – MDSPCs for the treatment of gentamicin-induced AKI.

© 2016 Elsevier Ltd. All rights reserved.

Contents

1. Introduction	802
2. Renal regeneration process after acute kidney injury	803
3. Mesenchymal stem cells in the treatment of acute kidney injury	804
4. Skeletal muscle derived stem progenitor cells and their application for renal regeneration	804
5. Conclusion	805
Acknowledgment	806
References	806

1. Introduction

Regenerative pharmacology and advanced therapy medicinal products is a relatively new and challenging field in drug development [1]. Acute kidney injury (AKI) is a frequent clinical event in nephrology with increasing incidence and a high mortality rate [2]. Due to hypoxic renal conditions, high metabolic demand, as well as frequent exposure to toxic agents, kidney are in a constant increased risk of acute injury [3]. AKI is characterized by acute

* Correspondence author at: Institute of Physiology and Pharmacology, Medical Academy, Lithuanian University of Health Sciences, Mickeviciaus Str. 9, Kaunas 44307, Lithuania.

E-mail addresses: egle.svitojute@ismuni.lt (E. Pavyde), arvydas.usas@ismuni.lt (A. Usas), romaldasmaciulaitis@vvt.lt (R. Maciulaitis).

Table 1
Mesenchymal stem cells for the treatment of acute kidney injury in different animal models.

Model	Species	Proposed mechanism	Reference
Bone marrow MSCs Gentamicin-induced AKI	Wistar rats	Paracrine effects, most likely through the RNA carried by the exosome-like microvesicles	Reis et al. [46]
Ischemia-reperfusion induced AKI	Albino rats	Migration into damaged tissue and differentiation	Sadek et al. [47]
Ischemia-reperfusion induced AKI	Cyclosporine-immunosuppressed Lewis rats	Decreased interstitial α -SMA accumulation and MMP2 activity, markers of fibroblast/fibroblast-like cell activation and renal remodelling	Alfarano et al. [48]
Glycerol induced AKI	Sprague-Dawley rats	Differentiation into renal tubular epithelial-like cells	Qian et al. [49]
Cisplatin-induced AKI	Sprague-Dawley rats	Inhibition of cell apoptosis	Qi et al. [50]
Cisplatin-induced AKI	Immunodeficient mice	Incorporation in the renal tissue, reduced renal cell apoptosis and increased proliferation	Morigi et al. [61]
Mercuric chloride-induced AKI	C57BL/6J and congenic eGFP expressing mice	Differentiation into endothelial cells of the peritubular region	Yadav et al. [62]
Adipose-derived MSCs			
Cisplatin-induced AKI	Sprague-Dawley rats	Anti-apoptotic effect	Yao et al. [51]
Folic acid-induced nephrotoxicity	FVB mice	Modulation of inflammation and cell cycle regulation	Burgos-Silva et al. [52]
Cisplatin-induced AKI	Sprague-Dawley rats	Suppression of oxidative stress and inflammatory reaction	Chen et al. [53]
Ischemia-reperfusion induced AKI	C57BL/6 mice	Reduced cytokine and chemokine expression	Furuichi et al. [54]
Cisplatin-induced AKI	Sprague-Dawley rats	Paracrine-protective effect, antiapoptotic capacity, decreased expression of inflammation-related molecules	Kim et al. [55]
Umbilical cord blood-derived MSCs			
Cisplatin-induced AKI	Immunodeficient mice	Regenerative and anti-inflammatory capacity, increased production of growth factors and inhibition of IL-1 β and TNF- α synthesis	Morigi et al. [59]
Ischemia-reperfusion induced AKI	C57BL/6 mice	Humoral effects and secretion of VEGF	Jang et al. [56]
Burn-induced AKI	Rats	Enhanced survival and prevention of apoptosis of resident kidney cells	Lu et al. [57]
Non-obese diabetic AKI	SCID mice	Reduction of apoptosis and promotion of renal tubular cell proliferation, mediated through the mitochondrial pathway, but independent of inflammatory cytokine effects and transdifferentiation	Fang et al. [58]
MSC-like stem cells from exfoliated deciduous teeth			
Ischemia-reperfusion induced AKI	C57BL/6 mice	Attenuation of inflammatory cytokine levels, reduction of MCP-1 and increase of HGF expression	Hattori et al. [60]

tubular necrosis, renal dysfunction, accumulation of metabolic waste products, which may lead to serious complications and failure of other organs [4]. AKI is most frequently caused by sepsis, nephrotoxicity or renal ischemia. The incidence of this complex clinical syndrome is rapidly increasing, especially among hospitalized patients in the medical and surgical intensive care units [2,5,6].

Despite the fact that in the past years the extensive effort has been made to develop new treatment techniques, supportive care and kidney transplantation remain the main treatment options for AKI. Dialysis serves only as a supportive care and may lead to severe morbidity [7], while transplantation therapy is limited by organ availability, possible immune reactions and the necessity for a lifelong use of immunosuppressants after transplantation [8]. This indicates the importance of the problem and the urgent need for new, innovative therapeutic modalities.

In this review, we will focus on the potential role of the extrarenal adult stem/progenitor cells in the kidney regenerative process, particularly on the mesenchymal stem cell lineages, including bone marrow, adipose and umbilical cord blood-derived MSCs for the treatment of AKI. The results of our study that initiated drug development using novel type of stem cells, skeletal muscle-derived stem/progenitor cells (MDSPCs), will be reflected in this review as well.

2. Renal regeneration process after acute kidney injury

AKI caused by ischemic or toxic conditions leads to renal dysfunction and loss of tubular epithelial cells. After injury, structural and biochemical alterations occur, resulting in vasoconstriction, separation of tubular cells and obstruction of tubules [9]. Morphologic changes due to renal damage can be defined as the loss of cell polarity and integrity of cytoskeleton, loss of brush border, epithelial cell barrier breakdown and tight junctions destruction, which may lead to the tubular cell apoptosis and/or necrosis [4,10].

The kidney has extensive regenerative capabilities, which are known for more than 60 years and are currently linked mainly to the population of resident progenitor cells. These adult renal progenitor cells (ARPCs) play an important role in the normal cell turnover and the repair of injured kidney. ARPCs were successfully isolated from the renal tubules, interstitium and Bowman's capsule, and in general have very similar characteristics [11–14]. These cells are characterized by the expression of CD24 (heat stable antigen), CD133 (prominin-1) and transcription factor Pax2. ARPCs were also found to be positive for the MSCs markers CD29, CD90, CD44, CD73 and negative for hematopoietic markers CD34 and CD45. ARPCs isolated from the Bowman's capsule differs from those isolated from the renal tubules by the positive expression of CD106. ARPCs can differentiate into various cell lineages (such as tubular epithelial cells, osteogenic cells, adipocytes) and have the potential to replace injured cells. However, the main mechanism

Download English Version:

<https://daneshyari.com/en/article/5557564>

Download Persian Version:

<https://daneshyari.com/article/5557564>

[Daneshyari.com](https://daneshyari.com)