PRETREATMENT OF RENAL SUPSCAPULAR ADMINISTRATION OF ADIPOSE TISSUE-DERIVED STEM CELLS AMELIORATE ISCHEMIA-REPERFUSION-INDUCED ACUTE KIDNEY INJURY

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Abstract

Background
Acute renal ischemic injury (AKI) represents a major clinical problem with renal arterial clamp at partial nephrectomy. The use of therapy using adipose tissue-derived stem cells (ASCs) has been suggested as a potential modality to attenuate the ischemic renal damage.

Methods
We investigated the possible reno-protection of pretreatment of ASCs before and after in a rat ischemia–reperfusion (I–R) model of AKI. Twenty-four hours post-ischemia, blood flow in peritubular capillaries (PTC) was measured using intravital videomicroscopy.

Results
We demonstrated that ADRC therapy significantly reduced serum creatinine and BUN. Histological analysis further validated a significantly attenuated tubular damage. Intravital videomicroscopy and measurement of red blood cell velocity in peritubular capillaries showed ASCs-injected kidneys displayed significant hemodynamic improvement.

Conclusions
The subscapular administration of ASCs to the kidney attenuates I/R renal injury though anti-inflammation, anti-apoptotic effect and peritubular capillary microcirculation. The present study suggests that ASCs would be a useful tool in preventing ischemic kidney damage in the clinical setting.

Key words: ADIPOSE TISSUE-DERIVED STEM CELLS; ISCHEMIA-REPERFUSION-INDUCED ACUTE KIDNEY INJURY; RENAL PROTECT; CYTOKINES

Background
Previous studies have demonstrated that administration of mesenchymal stromal cells (MSCs) accelerates the recovery of tissue injury in several organs including heart, liver, neuron, and pancreas. Administration of bone marrow-derived stromal cells (BMSCs) has also been shown to protect the kidney from AKI induced by cisplatin, glycerol, and ischemia-reperfusion injury. Recently, it has been demonstrated that MSCs can be obtained from adipose tissue. Like BMSCs, adipose tissue-derived stromal cells (ASCs) have the potential to differentiate into various types of cells and tissues. Previous studies suggest that ASCs may have an advantage over BMSCs. Firstly, adipose tissue is abundant, and can be obtained repeatedly with minimal invasive procedure. Secondly, the number of stem cells in the fat is greater than that in the bone marrow. Lastly, in general ASCs grow faster than BMSCs.

In a previous study, we reported renoprotection on and low serum cultured and non cultured ASCs and a transplanted endothelial cell for folic acid and cisplathin induced AKIs and acute
ischemia induced AKI\(^1\) and. Aim is to clarify the renoprotection of ASCs for ischemia induced AKI.

MATERIALS AND METHODS

Culture conditions

The basal culture medium was prepared as previously described\(^4\).

In vivo experimental subcapsular administration of hASCs

Subcapsular injection of \(2 \times 10^6\) of rat (r) 
-ASCs and control medium (Dulbecco’s modified Eagle’s medium, DMEM; Sigma-Aldrich) (each group \(n=6\)) was given to the left kidney of Acute kidney injury (AKI) rats. Blood samples were collected and blood urea nitrogen (BUN) and serum creatinine levels were measured by Mitsubishi Chemical Medience Co. Ltd (Tokyo, Japan). Rats were euthanized and renal cortical microcirculation was assessed using CCD video microscope\(^3\) and kidney samples were taken for the study.

Morphological analysis

To evaluate tubulointerstitial injury, Hematoxin Eosin (HE) and periodic acid Schiff (PAS) stained kidney sections were analysed using a quantitative grading.

Renal function

Rats treated with control medium demonstrated a marked rise in BUN and serum creatinine and, r-ASCs further suppressed the increase of serum creatinine (Figure 1).

Fig 1. Renal function after the intravenous injection of low serum cultured human adipose tissue-derived stromal cells (hLASCs).
Direct visualization of the renal cortical capillaries

The effects of r-ASCs on renal cortical microcirculation were examined by analyzing the direct images obtained with a CCD video microscope system. The blood flow velocity was significantly faster and the blood flow volume was greater in the r-ASCs group than in the control (Figure 2).

In conclusion, we demonstrate that subcapsular administration of r-ASCs protects the kidney via peritubular microcirculation from acute tubular injury.

References


