ERA-EDTA 50th Congress
Istanbul, Turkey
May 18-21, 2013
Ismail Acar, Not titled, 2011

Universidade Federal de São Paulo
UNIFESP
Universidade Federal de São Paulo

Supported by: FAPESP, CNPq, CAPES e FOR.

e-mail: vitoriaml@yahoo.com.br

CELL THERAPY WITH MESENCHYMAL STEM CELLS IN RENAL DAMAGE INDUCED BY IONIZING RADIATION IN AN ANIMAL MODEL

VITÓRIA MOREAU LONGO[1]; WALDEMAR SILVA ALMEIDA[1]; HELENA REGINA COMODO SEGRETO[2]; NESTOR SCHOR[1]
[1]-Nephrology Division, Federal University of São Paulo (UNIFESP). Brazil. [2]-Radiotherapy Department, Federal University of São Paulo (UNIFESP). Brazil.

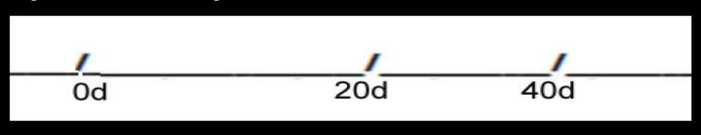
INTRODUCTION

Ionizing radiation (IR) causes cells death depending on the total irradiated dose and upon biological factors in the specific organ. The IR on the kidney's tissue induces time-depending systemic effects (hypertension, proteinuria, anemia, platelet aggregation, and others) as well as renal alterations (reduction glomerular function and diffuse sclerosis etc.). The reparative therapy with mesenchymal stem cells (MSCs) potentially can minimize renal injury alterations induced by IR. AIM: To evaluate the effect of therapy with MSCs in the renal lesions.

Division of Radiotherapy – HSP. **Irradiation at a dose of 8Gy on right Kidney** **MSCs from the femur and tibia** **Cell therapy 1X10⁶cells** **Animals kept warm to recover from anesthesia.**

METHODS

MSCs were obtained from male Wistar rats and characterized by FACS. We formed four groups of 9 animals each control (CTL); vehicle (V); ionizing radiation (IR) with a dose of 8Gy and, group treated with IR and cell therapy (IR+MSCs).



The rats were placed in metabolic cages for analysis of creatinine (CreatS, mg/dL), creatinine clearance (Clcreat, ml/min) and proteinuria (mg/24h) in the 20th and 40th days post-IR. We used immunofluorescence for Y chromosomal location and immunohistochemistry (IHC) for marking inflammation and fibrosis, in both periods.

Table 1: Biochemical analysis of blood samples and urine in the 20th day, in the control (CTL), vehicle (V), treated with radiotherapy (IR), treated with radiotherapy and mesenchymal stem cell (IR + MSCs).

Variable/group	CTL (n=9)	V (n=9)	IR (n=9)	IR+MSCs (n=9)
diuresis (ml/24h)	8,1±0,3	8,7±0,4	7,1±0,2	7,0±0,7
$Creat_S$ (mg/dL)	0,34±0,02	0,38±0,03	0,96±0,19*,#	0,42±0,04
Clearance (ml/min)	1,19±0,08	1,03±0,09	0,36±0,14*,#	0,79±0,12
Na^+_U (mEq/24h)	1,37±0,07	1,24±0,08	1,11±0,06	1,00±0,09

Values represent M±EP; $p<0,05$ *vs. CTL; V e #vs. IR- MSCs. Data were compared between groups by one-way analysis (ANOVA), followed by post hoc Student Newman Keuls.

RESULTS

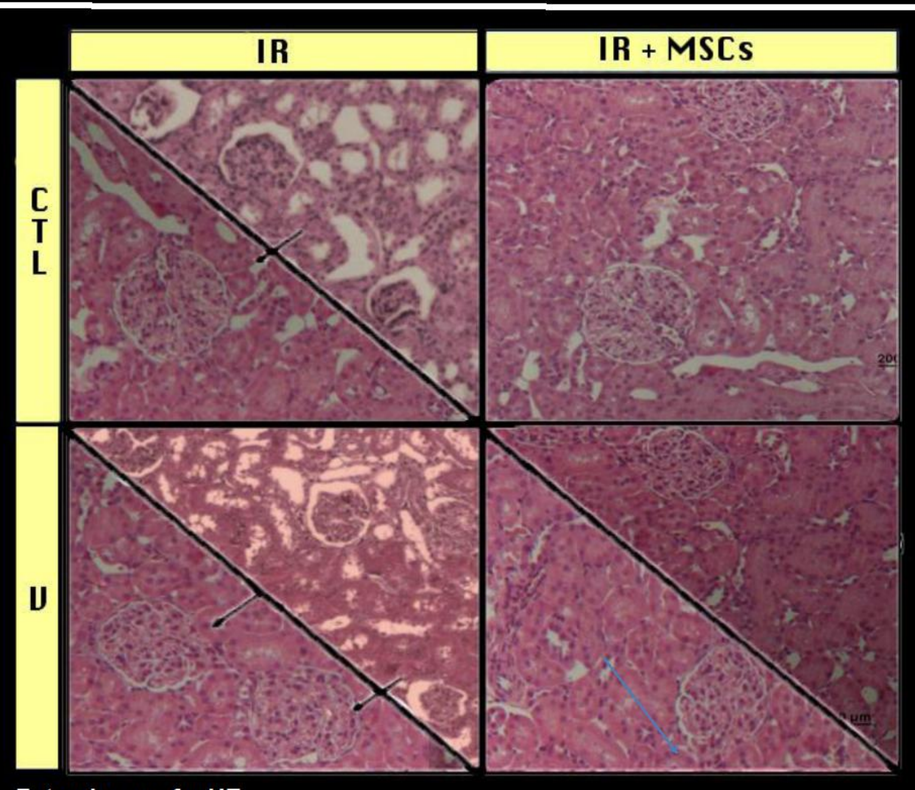
In day 20 when comparing groups IR and CTL, we found increase in mean Creat and reduction in Clcreat. Unlike occurred in relation to the IR group alone, animals that received MSCs presented lower CreatS and higher Clcreat.

In 40th day, the IR group showed an additional aggravation on renal function with significant increase in proteinuria when compared to the CTL and IR+MSCs, indicating that the renal function loss process is continuous and could blocked by MSCs transplantation. At 40th day of the evaluation there was a progressive impairments in the levels of CreatS and Clcreat in IR group, when compared to IR+MSCs and CTL, indicating that the protective effects of MSCs.

Table 2: Biochemical analysis of blood samples and urine in the 40th day, in the control (CTL), vehicle (V), treated with radiotherapy (IR), treated with radiotherapy and mesenchymal stem cell (IR + MSCs).

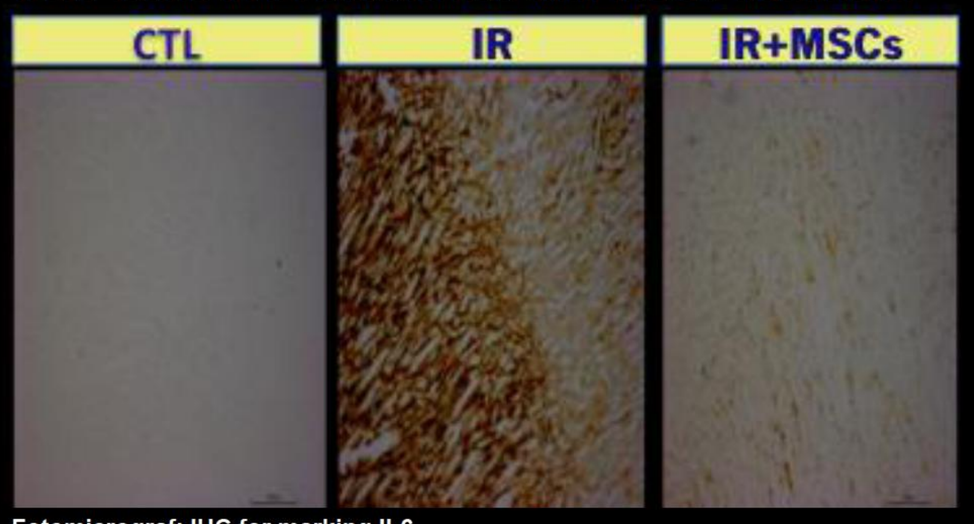
Variable/group	CTL (n=9)	V (n=9)	IR (n=9)	IR+MSCs (n=9)
Urinary volume (ml/24h)	8,2±0,3	8,4±0,2	25,9±2,7*,#	8,0±0,5
$Creat_S$ (mg/dL)	0,39±0,03	0,38±0,02	1,36±0,04*,#	0,41±0,04
Clearance (ml/min)	1,06±0,20	0,98±0,08	0,47±0,08	1,01±0,13
Na^+_U (mEq/24h)	1,21±0,09	1,10±0,08	3,86±0,42*,#	1,10±0,05
Na^+_S (mEq/L)	140,8±0,72	142±0,53	140,8±1,189	141,7±0,55
Fração de Na^+ (%)	0,7±0,09	0,6±0,06	4,3±0,59*,#	0,6±0,06
Urine Protein (mg/24h)	10,8±0,98	13,4±0,72	31,3±5,07*,#	13,4±1,69

Values represent M±EP; $p<0,05$ *vs. CTL; V e #vs. IR+ MSCs. Data were compared between groups by one-way analysis (ANOVA), followed by post hoc Student Newman Keuls.



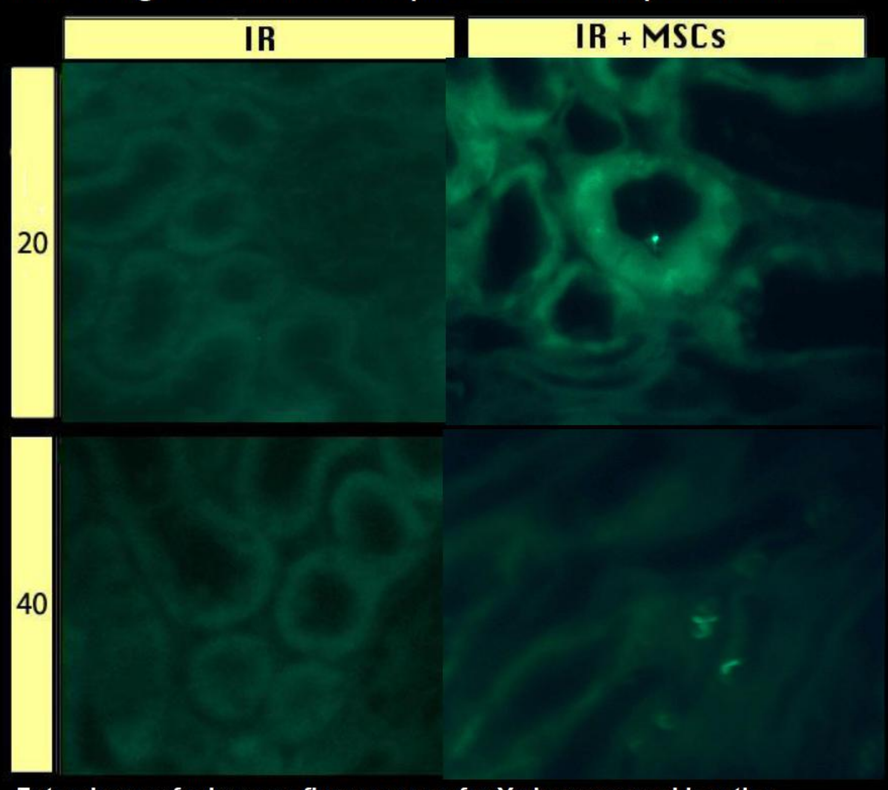
Fotomicrografy: HE.

Elevated levels of inflammatory marker for IL-6 were found in IR but blunted with MSCs treatment.



Fotomicrograf: IHC for marking IL6.

The Y chromosome was persistent in IR+MSCs, indicating a continuous process of reparation.



Fotomicrografy: immunofluorescence for Y chromosomal location.

CONCLUSION: Maintenance in Creats and Clcreat levels given by MSCs, in both periods were achieve. The Clcreat and proteinuria are normal after the 40th day in the RI+MSCs. The MSCs prevented the aggressive effect on renal function at 20 days post-IR, and attained normalcy after the 40th day. IHC showed that the presence of a chronic inflammatory process participate, as expected, in the development of this disease. The markup for IL-6 was absent in group IR+MSCs vs. IR, suggesting that MSCs prevented the aggressive effect of acute inflammation. The presence maintained of Y chromosome in IR+MSCs indicated persistence of the harmful inflammatory process despite no more IR aggression. Finally, the data showed that treatment with MSCs induced beneficial effects on the renal damage provoked by IR, and the MSCs transplantation induced beneficial effects in this experimental model.

DOI: 10.3252/pso.eu.50era.2013