**ACUTE KIDNEY INJURY – EXPERIMENTAL**

**FP204 CONTRAST MEDIA INDUCED NEPHROPATHY IN S.D. RATS: STUDY OF THE PREVENTIVE EFFECT OF MESENCHYMAL STEM CELLS**

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**Introduction and Aims:** Contrast-induced nephropathy (CIN) is a recognized complication in many diagnostic and interventional procedures with no available effective preventive measure apart from adequate hydration which is difficult in decompensated cardiac state. This study aimed to investigate the efficacy of mesenchymal stem cells (MSCs), as a promising therapy, in preventing CIN in rats.

**Methods:** 21 male Sprague Dawley (S.D.) rats weighing 200-300 gm were injected with ionic high osmolar contrast medium (Urograffin 76%) 8 mL/kg after 5 days gentamicin administration 100 ml/kg/day subcutaneous, then 24 hours water restriction followed by free water access for another 24 hours and then scarifying the rats. Rats were divided into 3 equal groups according to the type of injection given intravenously via the tail vein 48 hours prior to contrast medium injection; group I (+ve control) (0.5 ml 0.9% saline).

- **Group II (0.5 ml enriched culture media not containing stem cells).**
- **Group III (0.5 ml enriched culture media containing 3.5 million bone marrow-derived MSCs impregnated with iron ferumoxides (feridex) for 24 hours for assessment of kidney homing by prussian blue stain).** After sacrifice, blood samples were taken for measurement of serum creatinine (Scr), blood urea. One kidney was homogenized for assessment of glutathione reduced (GSH), lipid peroxide malondialdehyde (MDA) and superoxide dismutase (SOD) levels in kidney tissues. The other kidney was fixed for histopathological scoring for necrotic tubules, interstitial solid sheets of cells, regenerating tubules, mitotic figures, interstitial inflammatory cells, atrophic tubules and interstitial fibrosis and for immunohistochemical examination for caspase-3 (apoptotic marker) expression by counting all renal tubules immunoreactive for caspase-3 antigens.

**Results:** In group I, Scr 1.62 (range 0.75-3.8) mg/dl, blood urea 409 (range 107-574) mg/dl, MDA 22.6±4.8 nmol/gram (gm) tissue, GSH 6.15±1.43 gm/gm tissue, SOD 174±66.76 unit (U)/gm tissue. Histopathological examination revealed presence of high degree of tubular necrosis [3 (range 3-4)], caspase-3 expression and mild degree of the other parameters. Administration of enriched culture media in group II, compared to group I, resulted in significant reduction of Scr (P=0.01), urea (P=0.04) and caspase-3 expression, insignificant reduction of MDA, significant elevation in GSH (P=0.03), insignificant elevation in SOD and insignificant affection of all histopathological parameters.

Administration of bone marrow-derived MSCs in group III, compared to groups I, resulted in significant reduction of Scr (P=0.003), urea (P=0.006) and MDA (P=0.002), significant elevation in GSH (P=0.0001) and SOD (P=0.02) and significant reduction in the number of necrotic (P=0.01) and regenerating (P=0.04) tubules and caspase-3 expression. Compared to group II, MSCs resulted in insignificant reduction of Scr, significant reduction of urea (P=0.01) and MDA (P=0.002), significant elevation in GSH (P=0.001), insignificant elevation in SOD and significant reduction in the number of necrotic tubules (P=0.01) and caspase-3 expression. Iron labelled MSCs were not detected in kidney tissues.

**Conclusions:** We conclude that bone marrow-derived MSCs can prevent CIN in S.D. rats, giving a hope for a promising preventive and therapeutic tool for acute kidney injury.

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