

**EFFECTS OF HUMAN AMNIOTIC FLUID STEM CELLS ON CHRONIC BLADDER-ISCHEMIA ASSOCIATED CHANGES IN RAT BLADDER FUNCTION**

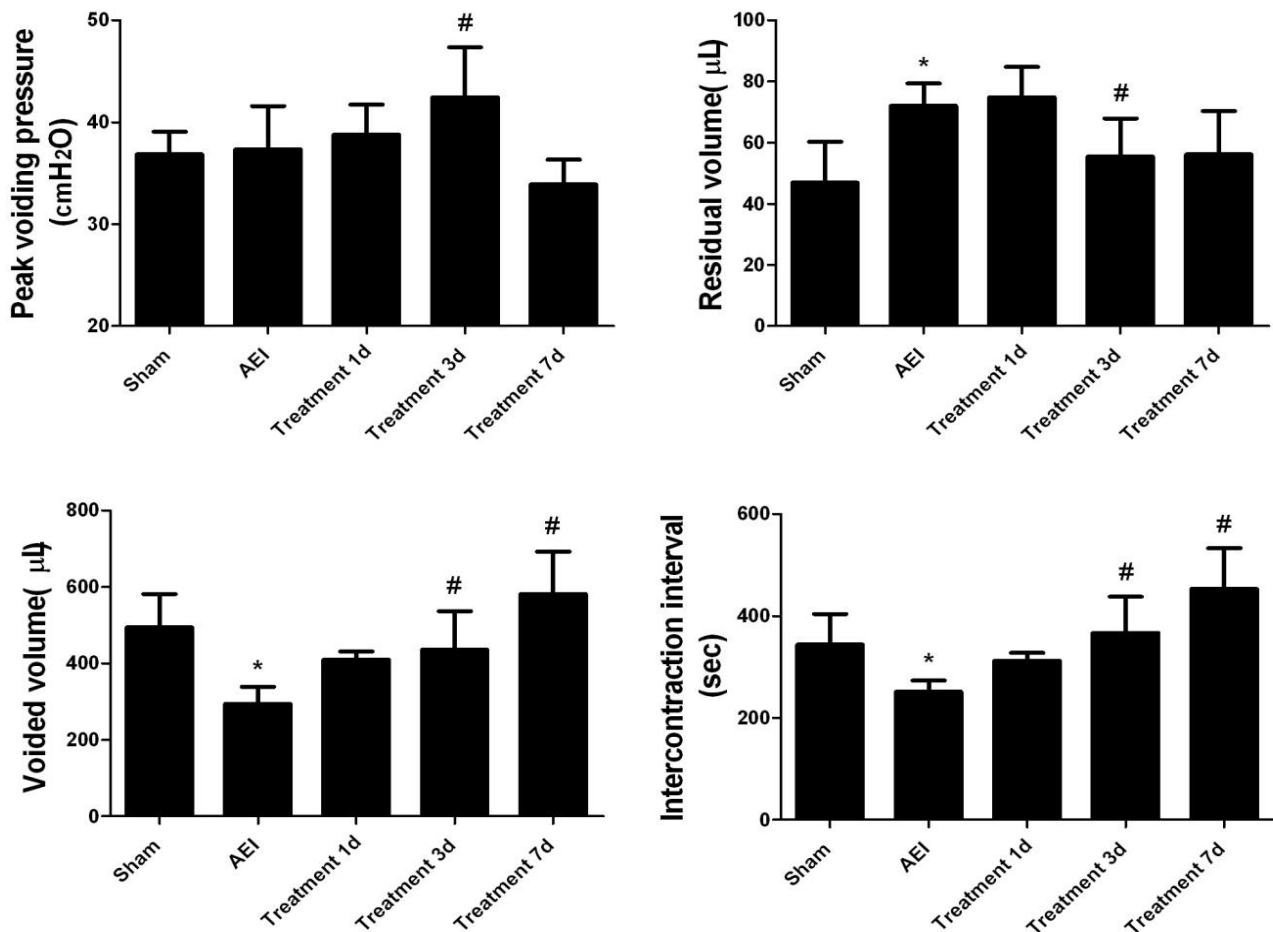
Hypothesis / aims of study

The precise mechanism responsible for lower urinary tract symptoms (LUTS) without bladder outlet obstruction still remains unclear. However, several studies suggested that a decrease in bladder blood flow resulting in chronic bladder ischemia may induce LUTS. Studies in rat models reported that oxidative stress and inflammatory processes might be related to the development of bladder dysfunction induced by chronic ischemia. Moreover, recent experimental data showed that stem cells transplantation may ameliorate impaired detrusor contractility in ischemia bladder. So, this study was conducted to investigate the effect of human amniotic fluid stem cells (hAFSCs) on the bladder dysfunction in a rat model of atherosclerosis-induced chronic bladder ischemia and its possible mechanism.

Study design, materials and methods

Adult female rats were subjected to either iliac arterial endothelial injury (AEI) or sham operation and received 2% cholesterol diet for 8 weeks. Fifty rats were divided into 5 groups: sham, AEI, AEI + one day hAFSCs treatment, AEI + 3 days hAFSCs treatment, and AEI + 7 days hAFSCs treatment. Bladder functions were analyzed by cystometry and iliac arteries histology were assessed at 8 weeks after AEI. The expressions of malondialdehyde (MDA), 8-hydroxy-20-deoxyguanosine (8OHdG), and tumor necrosis factor-alpha (TNF-α) were determined by immunohistochemistry.

**Fig. 1** Cystometric results in the experimental rats are presented (n = 10). AEI rats have an increase in residual urine and decrease in voided volume and intercontraction interval, compared to the sham group. After hAFSCs treatment done, AEI rats have a decrease in residual urine, and increase in voided volume, intercontraction interval and peak voiding pressure.



Results

AEI rats had increase in residual volumes, decrease in voided volumes and intercontraction intervals; however, these bladder dysfunctions improved after one, 3 and 7 days hAFSCs treatment (Fig. 1). When compared with sham rats, the average of common iliac arterial wall thickness in AEI rats were increased, but became significantly decreased after 3 and 7 days hAFSCs treatment. The expressions of 8OHdG and MDA in the AEI group had a significantly increase, compared to sham group. AEI rats had significant decrease in the expressions of 8OHdG, MDA and TNF-α after one, 3 and 7 days hAFSCs treatment.

### Interpretation of results

Our results showed that hAFSCs transplantation may ameliorate bladder dysfunction induced by chronic ischemia. Furthermore, as a noninvasive stem cell source, hAFSC is readily available from routine amniocenteses at the second trimester. HAFSC is multipotent and grow easily in culture and appear phenotypically and genetically stable.

### Concluding message

Bladder dysfunction caused by high-cholesterol and AEI-induced chronic bladder ischemia can be improved by hAFSCs transplantation that may be associated with the expression of oxidative stress and tumor necrosis factor.

### References

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### Disclosures

**Funding:** This work was supported by Chang Gung Memorial Hospital grant CMRP3D0961 and National Science Council of ROC grant NSC 103-2314-B-182A-101. **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Institutional Ethics Committee for the Care and Use of Experimental Animals and the Institutional Review Board of Chang Gung Memorial Hospital.