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EFFECT OF PROLYL 4-HYDROXYLASE INHIBITOR ON THE BLADDER FUNCTION, BLADDER HYPERTROPHY, AND EXPRESSSION OF PROLYL 4-HYDROXYLASE, COLLAGEN SUBTYPE IN THE RAT MODEL WITH PARTIAL BLADDER OUTLET OBSTRUCTION

Hypothesis / aims of study
This study was performed to investigate prolyl 4-hydroxylase (P4H) inhibitor (2,4-diethylpyridine dicarboxylate)-mediated effect on the bladder function, bladder hypertrophy, and expressions of P4H and collagen subtype in the rat with partial bladder outlet obstruction (pBOO).
Study design, materials and methods
Twenty female Sprague-Dawley rats (200-250g) were divided into three groups; pBOO with P4H inhibitor 20mg/kg (group A1, A2, each n=5), pBOO with normal saline (group B1, B2, each n=5), and normal control (group C1, C2, each n=5). After pBOO for 1 and 2 weeks in A, B, and C groups, each amount of inhibitor was administered orally once a day for 2 weeks. After total 3 and 4 weeks, the bladders in all group were removed following to cystometry. To evaluate the changes due to pBOO and P4H inhibitor, the cystometry study, Masson's trichrome stain for muscle change and immunohistochemical stain for P4H, collagen subtype expression were performed in all group.
Results
The pressure and volume parameter in cystometry of pBOO group A and B increased significantly than normal group C ($p<0.05$), and that of group A decreased significantly than group B ($p<0.05$). Masson's trichrome stain demonstrated that the muscle thickness of pBOO group A and B increased significantly than normal group C ($p=0.0001$), and compared with that of the group B ($p=0.008$), the group A had substantially reduced muscle thickness. Based on immunohistochemical stain, P4H expression in group A2 and B2 was augmented compared with C2 group ($p=0.002$), and furthermore, it was down-regulated in P4H inhibitor groups than in group B2 ($p=0.003$). pBOO led to the increasing collagen I and III protein expression compared with C2 group ($p=0.05$ and $p=0.003$), and those in group A2 marginally decreased compared with those in group B2 ($p=0.135$ and $p=0.811$). The ratio of collagen I/III was 1.9, 2.4 and 1.2 in group A2, B2, and C2, respectively.
Interpretation of results
In the rat with pBOO, P4H inhibitor improved on the bladder function in cystometry, and decreased bladder hypertrophy, and expressions of P4H and collagen subtype.
Concluding message
Our data suggest that the P4H inhibitor may be helpful to improve bladder function and to reduce the bladder fibrosis caused by pBOO.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**ethics committee at College of Medicine, Pusan National University**