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ALFUZOSIN, BUT NOT TAMSULOSIN, RELIEVES BLADDER HYPERTROPHY IN RATS DESPITE A PERSISTENT BLADDER OUTLET OBSTRUCTION

Hypothesis / aims of study

A pro-apoptotic effect on bladder wall (1) and prostatic tissue (2) was reported in BPH patients treated with α_1-adrenoceptor blockers (α_1-AR). The aim of the present study was to evaluate the effects of a chronic treatment with alfuzosin (ALF, 3 and 10 mg/kg/day), a quinazoline derivative, and tamsulosin (TAMS, 1 and 3 mg/kg/day), a sulphonamide derivative, on bladder hypertrophy induced by bladder outlet obstruction (BOO).

Study design, materials and methods

In female rats a ligature was tied around the urethra leaving a 1 mm diameter lumen. Six weeks later, Alzet® osmotic pumps filled with ALF, TAMS or vehicle were implanted subcutaneously in the obstructed (OBS) rats. After 7 days-treatment rats were sacrificed and bladders were collected. Bladders were weighted (BW) and histomorphometric analyses were performed on Sirius red colorations to determine muscularis layer thickness (MLT) and muscle density (MD). TUNEL assay and PCNA staining were used to evaluate apoptotic index (AI) and proliferation in the bladder wall, respectively.

Results

OBS vehicle-treated rats displayed a significant increase in BW, MLT and MD as compared with sham rats as well as a significant decrease in AI. At the highest dose tested, ALF significantly decreased BW, MD towards quasi-normalization *vs* sham-operated animals, and increased AI. ALF was devoid of significant effect on MLT and proliferation. TAMS had no significant effect on any parameter studied. (Figure)

Interpretation of results

In contrast to TAMS, one-week treatment with ALF, at non-hypotensive doses (3), relieves the bladder hypertrophy associated with BOO. This effect is not due to a decreased obstruction at the urethral level since the urethral ligature was present during α_1-AR administration. The decreased bladder hypertrophy observed with ALF at 10 mg/kg correlates with the decreased MD in the bladder wall and the increased AI.

Concluding message

These results suggest that ALF counteracts the bladder hypertrophy induced by BOO in rats, and that these effects appear already after one week treatment. Since TAMS was devoid of such effects, we conclude that this effect of ALF could be related to its quinazoline structure. This could have clinical significance in the management of LUTS associated with BOO.

References

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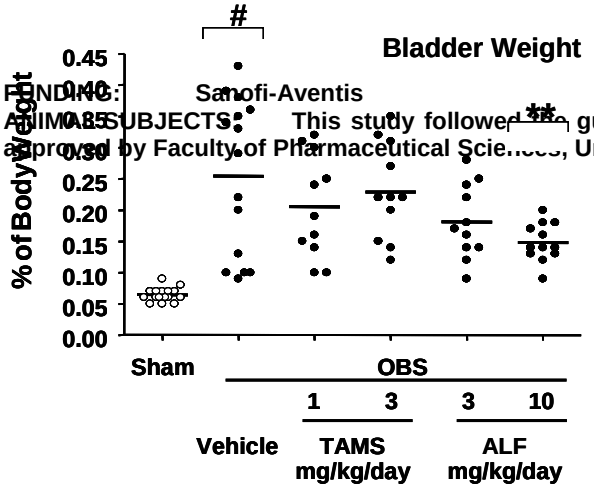

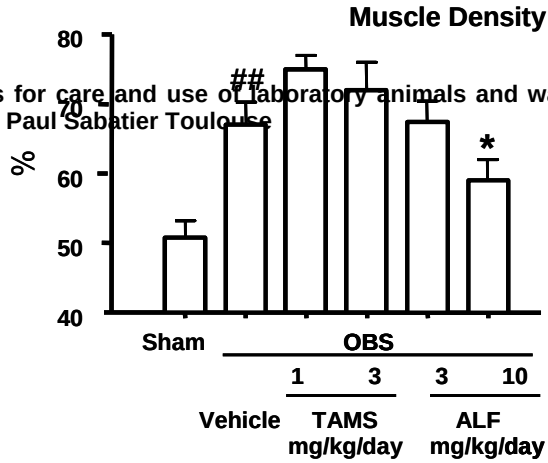

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ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by Faculty of Pharmaceutical Sciences, University Paul Sabatier Toulouse

Student *t*-test. ## p<0.001, # p<0.01 *vs* Sham