The corresponding values for V are shown below by in Figure 2. As indicated DHT produces a significant ($p<0.05$) decrease in V in comparison to baseline values. However when TAD is co-administered, the reduction in V is supressed and when TAD is post-administered the reduction in V is reversed.

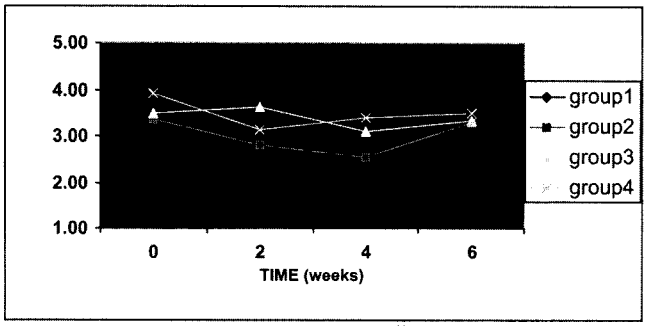
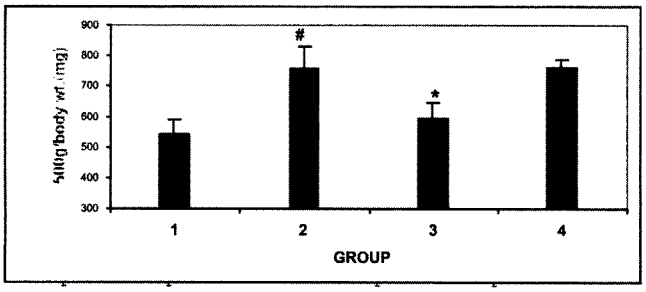


Figure 2 Comparison between baseline and 4th week of group 2 *p<0.05



2&3

Figure 3 shows the effect of treatment on the weight of the prostates showing that DHT produces a significant increase ($p<0.05$) in prostate weight compared to controls. As indicated, co-treatment with TAD, group3, significantly suppresses ($p<0.05$) prostate growth in comparison to DHT in SO; group2. Furthermore in comparison to DHT-treatment group2, post-treatment with TAD, group4, does not significantly change prostate weight.

Conclusion

These results clearly demonstrate that both the co- and post-treatment with oral TAD can significantly suppress the DHT-induced effects on the frequency/volume characteristics of micturition in the conscious rat. The most pronounced effect of TAD was observed in its influence on the frequency of micturition providing evidence to suggest amelioration of the " obstructive micturition characteristics" as induced by experimental prostate growth using DHT. Finally it is suggesting that, co-TAD but not post-TAD administration regresses DHT-induced prostate growth.

SUPPORTED BY FOURNIER LABORATORIES

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

CHANGES IN MICROVESSEL DENSITY IN THE PARTIALLY OBSTRUCTED RAT BLADDER

Aim of Study: Experimental partial infravesical obstruction leads to a series of bladder physiologic and architectural changes that occur during a progression from initial bladder compensation to a decompensated state. During the early acute phase of obstruction, increased wall tension and bladder stretch during the storage and emptying stages causes a reduction in bladder perfusion (ischemia) [1].

Ischemia is a potent stimulus of angiogenesis, which is a known prerequisite for neoplastic proliferation and likely plays a similarly significant role in permitting benign tissue hypertrophy [2,3] The purpose of this study was to investigate the neovascular changes that occur in rat bladder following partial infravesical obstruction.

Methods: Adult female rats were anesthetized and surgically opened to expose the bladder and proximal urethra. A 3 Fr catheter was placed per urethra, and the catheterized proximal urethra was ligated with a 4-0 silk suture to create a fixed 1 mm internal diameter partial obstruction. Rats were sacrificed at 4, 7 and 21 days. Their bladders were weighed and frozen in liquid nitrogen. Histological sections were immunostained for the endothelial cell marker Factor VIII (vWF). Positively staining non-contiguous clusters of cells were counted in the submucosa and muscle wall areas for each bladder. Longitudinal and horizontal dimensions of bladder wall, submucosa and luminal surfaces were measured for surface area calculation. Microvessel density is reported as number of vessels per calculated square millimeter surface area.

Results: Partial infravesical obstruction resulted in an average increase in bladder mass of 298% and 598% at 7 and 21 days respectively. The absolute number of microvessels in both submucosa and muscle layers increased in early obstruction (4 – 7 days), but in both cases returned to normal levels after three weeks (Figures 1 and 2). Microvessel density in the submucosa of partially obstructed rat bladders decreased in the initial post-obstructive stage before rebounding to near-normal levels after three weeks (Figure 1). In contrast, microvessel density in the muscle wall of obstructed rat bladders did not return to normal levels, but rather steadily declined over time (Figure 2).

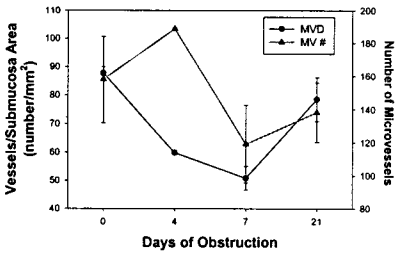

Figure 1: Bladder submucosa microvessel density (MVD) and absolute number of microvessels (MV #) per section following partial bladder outlet obstruction. Bars represent mean ± standard error.

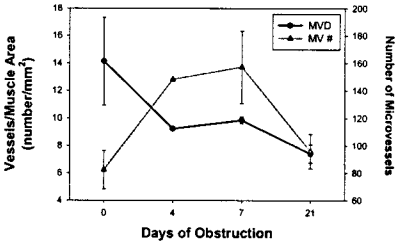

Figure 2: Bladder muscle wall microvessel density (MVD) and absolute number of microvessels (MV #) per section following partial bladder outlet obstruction. Bars represent mean ± standard error.

Conclusions: Adequate perfusion of growing tissue is necessary for maintaining normal physiologic function. In the cardiac, skeletal, and enteric smooth muscle systems, ischemia and even simple stretch are known to be sufficient stimuli of angiogenesis [4,5,6]. This study demonstrates that an angiogenic response to partial infravesical obstruction occurs in bladder submucosa and muscle layers 4 – 7 days following obstruction. In the bladder submucosa layer, this neovascularization helps restore microvessel density to near-normal levels by three weeks post-obstruction. However, the bladder muscle neovascular response to partial infravesical obstruction is inadequate to maintain normal microvessel density in the face of progressive bladder hypertrophy. This may result in a state of chronic detrusor ishemia in the obstructed bladder, and thus contribute to bladder decompensation occurring in the setting of long-term bladder outlet obstruction.

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

PROTECTIVE EFFECT OF DIET HIGH IN VITAMIN E ON BLADDER FUNCTION SECONDARY TO PARTIAL OUTLET OBSTRUCTION

Aims of Study: Vitamin E is a widely used dietary supplement and an anti-oxidant. The specific aim of this study was to determine if diet high in vitamin E in rabbits reduced either the hypertrophic response of the bladder to partial outlet obstruction or the accompanying contractile dysfunction.

Methods: Twenty-four male New Zealand rabbits (3 to 5 kg.) were randomly separated into 4 groups of 6 rabbits each. Each rabbit in-group 1 and 2 received diet high in vitamin E for 4 weeks, while each rabbits in-group 3 and 4 received normal diet. Four weeks later, each rabbit in-groups 2 and 4 underwent partial outlet obstruction of the bladder as previously described (1,2). At three weeks of obstruction (obst), each rabbit was anesthetized and the bladders excised. In-vitro contractility studies were performed and the balance of the bladder frozen and analyzed for MDA.

Results: 1) Diet high in vitamin E significantly reduced the effect of partial outlet obstruction on the bladder mass. Obstructed bladders of rabbit on normal diet weighed almost 8 times greater then control, while the obstructed bladders of rabbits on diet high in vitamin E weighed only 2.5 times greater then control.

2) Diet high in vitamin E resulted in significant protective effect on the maximal contractile response and on the rate of maximal contractile response to field stimulation (FS = 32 HZ), Adenosine Tri-phosphate (ATP), carbachol and KCl. See table below.

	FS 32 Hz		ATP		Carbachol		KCl	
% Decline in:	Obst. N D	Obst. E D*	Obst. N D	Obst. E D*	Obst. N D	Obst. E D *	Obst. N D	Obst. E D *
Max. Tension	55	17	42	9	38	3	35	0
Rate of Tension Generation	61	36	61	35	57	4	41	33

N D = Normal Diet; E D High E diet; * = Compared to respective normal diet

3) Obstruction stimulated a significant increase in MDA content in the microsomal particulate fraction. Diet high in vitamin E significantly reduced the basal levels of Malondialdehyde (MDA) in both microsomes and mitochondria by 60%. This reduction was seen in control and obstructed group on high E diet. And more importantly MDA levels in control and obstructed rabbits on high vitamin E diet were identical.

Conclusion: These results clearly demonstrate that diet high in vitamin E reduced the hypertrophic response of a partially obstructed bladder and protracted the bladder from contractile dysfunctions induced by the partial outlet obstruction. This protection in part is provided by the reduction in the level of lipid peroxidation.

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