Can 5-alpha reductase inhibitor induce fibrosis in human prostate hyperplasia?

Chen zhao, M.D., Jong Kwan Park, M.D., Ph. D.

Department of Urology, Medical School, and Institute for Medical Sciences, and Research Institute and Clinical Trial Center of Medical Device of Chonbuk National University Hospital, Jeonju, Korea
Introduction

• The development of BPH is an androgen-dependent process.

• Androgen suppression causes regression of the epithelial elements of the prostate, resulting in a reduction in the size of the gland and improvement in symptoms.

• 5ARIs, finasteride and dutasteride, inhibit 5 AR, an enzyme that catalyzes the irreversible reduction of testosterone (T) to dihydrotestosterone (DHT).
Introduction

Androgen deprivation is associated with penile cavernosal fibrosis resulting in

• penile tissue atrophy
• alterations in dorsal nerve structure
• alterations in endothelial morphology
• reductions in trabecular smooth muscle content
• increases in deposition of extracellular matrix
Introduction

Transforming growth factor-β (TGF-β) signaling pathway plays the most important role in the fibrotic process

- TGF-β reduces collagenase production
- and stimulates the expression of tissue inhibitor of metalloproteinases
- resulting in an overall inhibition of extracellular matrix (ECM) degradation
- leading to excessive matrix accumulation
To evaluate whether the transforming growth factor-β (TGF-β) signaling pathway was activated in human hypertrophied prostate treated by 5 ARIs.

- 32 BPH patients underwent TURP enrolled
- Groups:
  - Group 1: treated with tamsulosin for 2 years
  - Group 2: treated with combination of tamsulosin and dutasteride for at least 1 year
- Western blotting:
  - nNOS, iNOS, eNOS,
  - TGF-β1, TGF-β2,
  - p-Smad2/3,
  - E-cadherin, N-cadherin,
  - α-smooth muscle actin
- EIA: TGF-β

*Significant difference between Group 1 and Group 2.
Conclusion

• Long time treatment with 5 ARI increases the risk of fibrosis by the TGF-β-Smad signaling pathway.

• This fibrosis is accompanied by the induction of iNOS, which acts as an endogenous antifibrotic mechanism in response to the profibrotic processes.

• eNOS decreased in lateral prostate but not anterior fibromuscular portion.

• nNOS may contribute to prostate smooth muscle relaxation and improve the symptoms.
Thank you for your attention!