Testosterone protects from metabolic syndrome-associated prostate inflammation: an experimental study in rabbit


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INTRODUCTION and OBJECTIVE
A strong relationship between metabolic syndrome (MetS), benign prostatic hyperplasia (BPH)/lower urinary tract symptoms (LUTS) has been documented. A common denominator at play is hypogonadism. However testosterone supplementation is limited by concerns for its potential risks on prostate health. The aim of the study is to evaluate whether MetS-associated prostate alterations are prevented by in vivo testosterone supplementation.

EXPERIMENTAL DESIGN

Animal model of MetS

- Mice rabbits
- High fat diet (HFD) with 0.5% cholesterol and 4% peanut oil
- Mice rabbits + testosterone
- Testosterone (30 mg/week)

In vitro experiments using human prostatic stromal cells, hBPH, previously characterized [Penna et al. Prostate 2009; Fibbi et al. J Sex Med 2009]

Cell treatments: after 24-hours serum starvation, hBPH were exposed to increasing doses of DHT (10^{-11}-10^{-7}M) and then were stimulated with TNFα (10 ng/ml) for 5 hours. Untreated cells were used as control. Culture media were collected for analysing cytokine secretion. Cells were collected for measuring protein content.

Cytokine release analysis: Bio-Plex Assays (Bio-Rad Laboratories, UK) was used for multiple assay of cytokine quantitation released in culture media by hBPH.

NFκB activation: nuclear translocation of NFκB was evaluated with immunocytochemistry in hBPH.

RESULTS

HFD rabbits showed prostatitis-like alterations, all prevented by T supplementation, such as:

1) Prostate fibrosis (masson-trichrome staining)

2) Hypoxia Hypoxyprobe immunostaining

3) Lymphocyte infiltration formation of corpora amylacea (haematoxylin/eosin staining)

4) Increased expression of inflammatory markers (quantitative real time PCR)

5) Increased expression of fibrosis/myofibroblasts activation markers (qRTPCR)

6) Negative association of testosterone/estriol ratio with fibrosis and inflammation in the prostate of MetS rabbits

7) Pretreatment with DHT inhibits secretion of cytokines and chemokines and growth factors by hBPH cells

8) NFκB nuclear translocation in BPH is inhibited by DHT pretreatment

CONCLUSIONS

These data highlight that testosterone supplementation could have a beneficial effect on prostate health by counteracting MetS-related prostatic alterations such as hypoxia, fibrosis and inflammation which are the key components in the development and progression of benign prostatic hyperplasia and LUTS.