Point-Counterpoint:

Are We Ignoring Level One Evidence by Not Prescribing Appropriate Medical Therapy?

~ E. David Crawford, MD

Alternative Medicine Should Be the Choice

~ Mark A. Moyad, MD, MPH

CAM Should be the Choice: Can we really do any worse compared to the damage already done?

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Heart Healthy=Prostate Healthy

Heart Healthy=Prostate Healthy=Colon Healthy=Breast Healthy…

Moyad MA. Urol Nurs 2003;23(6):439-441.

BPH

Lifestyle factors

- Diet (energy restriction, fat, fruits & veggies…)
- Physical activity (HDL…)
- Obesity (BMI…)
- Hyperinsulinemia
- Smoking
- Other (age, height, HTN, vit. D…)

Moyad MA, Lowe FC. Am J Med 2008; 121 (8 Suppl 2):S34-S42.

Health Professionals-I

- N=51,529 men
- Mean age=53 +/- 9 years
- 8 yrs of follow-up
- Total cases=3523 (Surgery &/or AUA score)
- Noncases=24,388 (AUA score $\leq$7)

Suzuki S, et al. Am J Clin Nutr 75:689-697, 2002.

Health Professionals-II

- Total energy intake=51% increase
- Total dietary fat=No difference
- Increase in sympathetic activity?
- Increase in testosterone?
- Increase in abdominal obesity? Aromatization?

Bottom Line=Largest observational study.

Diet & BPH

- Higher caloric consumption=Higher risk
- Higher meat consumption=Higher risk
- More omega-3 fatty acids=Lower risk
- More fruits & veggies=Lower Risk

Bottom Line=Heart healthy=Prostate Healthy!!!

Koskimaki J, et al: Scand J Urol Nephrol 34:46-50, 2000. Yang YJ, et al: Clin Biochem 32:405-409, 1999.

Physical activity & BPH

- Health Professional Follow-up
- Walking=2-3 hours/wk=25% lower risk
- Total BPH (& surgery & symptoms)

Bottom Line=Walking/physical activity is good for your prostate.

Platz EA, et al: Arch Intern Med 158:2349-2356, 1998.

Exercise vs. Zoloft®

- Duke Trial, n=156, MDD
- 4 months-exercise (3x), zoloft® (150 mg), both
- Baseline, 4 & 6 months post-study
- 50% reduction w/exercise

Bottom Line=Zoloft® fast-exercise more effective.

Blumenthal, et al. Arch Intern Med 159:2349-56,1999./ Babyak,et al. Psychosom Med 62:633-8, 2000.

E=Exercise (resistance) (Bone Loss & LHRH?)

Increase:
-GH
-DHEA
-WBC…

- Australia Study (10 men, age=70)
- 20 wk high-intensity resistance exercise (5 months)
- 5 men on acute & 5 on chronic ADT

- Increased Muscle Strength, No change in Fat Mass
- No bone loss at any site + No Hgb change!

Bottom Line=Exaggerated? Moyad Experience.

Galvao DA, et al. (Spry N, Newton R…). Pros Cancer Prostat Dis, 2006.

Obesity & BPH

- Health professionals, Korean study
- Higher WHR/ waist circumference (≥43 vs <35 inches)
- Lower HDL

Bottom Line=WHR or waist circum= BPH risk (OR=2.38)

Giovannucci E, et al Am J Epidemioll 140:989-1002, 1994. Lee E, et al: Br J Urol 79:736-741, 1997

Smoking & BPH

- Population study (n=2100)
- OR=1.47 (current smokers)
- OR=1.38 (former smokers)
- Changes hormone levels (ATBC…)

Bottom Line=Reversible w/smoking cessation?

Koskimaki J, et al: J Urol 159:1580-1582, 1998.

Hyperinsulinemia & BPH

- Swedish study of 307 consecutive patients
- Annual BPH growth rate=higher in men with higher plasma insulin levels.

Bottom Line=Type II diabetes, HTN, obesity, & dyslipidemia=greater prostate growth.

Hammarsten J, Hogstedt B:Eur Urol 39:151-158, 2001.

Hyperinsulinemia/obesity & Urology

- BPH
- E.D.
- Prostate cancer
- Renal cell carcinoma (RCC)…

Bottom Line=Obesity epidemic=Urology case epidemic=Marriage of urology & preventive medicine.

Moyad MA: Urology January, 2002.

BPH

Supplements

- Saw palmetto (Serenoa repens=Sabal serrulata)
- Pygeum africanum (African plum)
- B-sitosterol (Hypoxis rooperi)
- Cernilton (Secale cercale=rye pollen)

Lowe FC, et al: Prostate 37:187-193, 1998. Moyad MA: Urol Clin N America, 2001.

Plant extract components of BPH supplements

- Phytosterols
- B-sitosterol
- Alpha-5-sterols
- Alpha-7-sterols
- Campesterol
- Stigmasterol
- Lupenone

Lowe FC, et al: Prostate 37:187-193, 1998. Moyad MA: Urol Clin N America, 2001

Plant extract components cont.

- Lupeol
- Terpenoids
- Fatty acids
- Lectins
- Plant oils
- Polysaccharides
- Flavonoids

Lowe FC, et al: Prostate 37:187-193, 1998. Moyad MA: Urol Clin N America, 2001

Plant extract components cont.

- Phyto-estrogens
- Coumestrol
- Genistein
- Daidzein
- Bowman-Birk inhibitor

Lowe FC, et al: Prostate 37:187-193, 1998.

Potential mechanisms of BPH supp & Lifestyle Changes.

- Placebo effect (1/3rd rule)
- Antiinflammatory
- Cholesterol absorption & metabolism
- SHBG
- Inhibition of 5-alpha-reductase
- Inhibition of aromatase
- Other antiandrogenic and/or antiestrogenic effects

Potential mechanisms cont.

- Detrusor function improvement
- Effect on growth factors=antiproliferative effects
- Block alpha-adrenergic receptors
- Free radical scavengers

Lowe FC, et al: Prostate 37:187-193, 1998. Moyad MA: Urol Clin N America, 2001.

Saw palmetto (meta-analysis)

- 18 randomized trials (n=2939)-Permixon®
- Decreased symp. scores, nocturia,peak urine flow
- Similar to finasteride

Bottom line=Mean study duration=9 weeks???

Wilt TJ, et al: JAMA 280:1604-1609, 1998

Saw palmetto (meta-analysis)

- Mean dose=320 mg/day
- No PSA change at this dose, 1-2% E.D. rate
- Use in Europe decreasing (Insurance???)

Bottom line=Mechanism of action???

Wilt TJ, et al: JAMA 280:1604-1609, 1998

Saw palmetto-UCLA

- N=44 (age 45-80), 6 months vs. placebo & finast.
- Clinical parameters not different from placebo
- Epithelial contraction

Bottom line=Mechanism of action???

Marks LS, et al: Urology 57:999-1005, 2001

Saw palmetto-mild finasteride or dutasteride effect?

	Finasteride	Saw palmetto
PSA	50% decrease	No change
DHT	70% decrease	No change
Testost.	10-20% increase	No change
Gland-vol.	20% decrease	No change
Epith. (%)	55% decrease	40% decrease
Gland-DHT	80% decrease	32-50% decrease
Gland-Tes.	5-10x increase	0-125% increase

Marks LS, et al: Urology 57:999-1005, 2001.

Permixon® vs. Tamsulosin-I

- 1 yr (n=542 from an n=704)
- 320 mg/day vs. 0.4 mg/day
- IPSS $\geq$ 10
- 11 European countries
- BMI=26-27
- Age=65 years

Debruyne F, et al. European Urology Annual Meeting, 2002.

Permixon® vs. Tamsulosin-II

- Equivalent results
- IPSS=-4.4
- Qmax=similar=1.8-1.9 mL/s
- No diff in irritative vs. obstructive sympt improve
- PSA stable + prostate vol decline w/permixon
- Ejac. Disorders=0.6% vs 4.2%

Debruyne F, et al. European Urology Annual Meeting, 2002.

Saw palmetto=hair tonic…?

- Inhibits 5-alpha reductase type II & I???
- Similar to propecia® & avodart®???
- Prostate cancer prevention=PCPT Trial???
- COX-inhibition???

Bottom line=millions in sales=an option

Moyad MA: Urol Clin N Am Feb, 2002.

Pygeum africanum (meta-analysis)

- Extract-bark of African plum evergreen tree
- 18 randomized trials (n=1,562 men)-Tadenan®
- Mean study=64 days (range 1-4 months)-100 mg

Bottom Line=Modestly but significantly improves urologic symptoms & flow measures. Long term?

Ishani A, et al: Am J Med 109:654-664, 2000.

B-sitosterol

- Extract of African star grass=Harzol®
- >70% dry weight=B-sitosterol (cholesterol?)
- 6 month trials (benefits up to 18 months)
- No effect on prostate size (stromal TGFbeta?)

Bottom Line=20 mg tid-symptoms not obstruction.

Berges RR, et al: BJU Intl 85:842-846, 2000.

Cernilton® (rye-grass pollen)

- Prostatitis and/or BPH
- Not improve flow rates, residual vol., prost. size
- Improves symptoms-esp. nocturia (anti-inflamm)
- N=444 (2 trials) 3-6 months

Bottom Line=60 mg tid for prostatitis. BPH?

Macdonald R, et al: BJU Intl 85:836-841, 1999.

Quercetin

- Naturally occurring bioflavonoid
- High conc. in red wine, onions, green tea
- Anti-oxidant
- Tyrosine kinase inhib.
- Nitric oxide inhibitor
- Anti-inflammatory….(COX…)

Moyad MA: Urology January, 2001

Quercetin trial

- N=30
- 500 mg twice daily vs. placebo (1 month)
- Non-bacterial chronic prostatitis
- NIH chronic prostatitis symptom score

Shoskes DA: Urology 54:960-963, 1999

Quercetin trial

	Placebo	Quercetin
Age (yr)	43.5	46.2
Symp. Duration	11.5 yr	10.5 yr
Initial WBC/hpf	13.1	16.9
Final WBC/hpf	8.3	2.9
NIH symp. Score (pain,urin,QOL)	20.2 to 18.8	21.0 to 13.1 (significant)

Shoskes DA: Urology 54:960-963, 1999

Quercetin-Conclusions

- Case-series
- 1 randomized small trial for 1 month
- Prosta-Q® (quercetin, bromelain, papain,…)
- Wine, green-tea??? Why not.

Bottom Line=Conflict of intererst? Be careful-Walmart sells it for 50-75% less. Cysta-Q®……

Shoskes DA: Urology 54:960-963, 1999

Cernilton®-Pollen extract

- 1 tablet tid (180 mg)-6 months (n=90)
- Similar results to quercetin trial
- Reduction in WBC,
- Decrease in complement C3 in ejaculate

Bottom Line=Cernitin company of Ohio. Prostaglandin & leukotriene inhibitor?…

Rugendorff EW, et al: BJU 71,433-438, 1993.

BPH & Prostatitis-Bottom Line

- Lifestyle changes=Primary Prevention
- Saw palmetto=320 mg/d (Quality control…)
- Pygeum africanum=100 mg/day
- B-sitosterol (Af. star grass=Harzol®)-20 mg TID
- Cernilton®=rye grass pollen=60 mg TID
- Quercetin=Prosta-Q®?=500 mg BID

Risk factors for ED

- Alcohol abuse
- Anemia
- CHD or PVD
- Depression
- Drug abuse
- Endocrine disorders
- Hyperlipidemia
- Hypertension
- Hypogonadism
- Peyronie's disease
- Smoking
- Trauma (bike seats??) or surgery to the pelvis or spine
- Vascular surgery

Moyad MA. Contemp Urology: submitted.

Lifestyle & ED

- N=1156, follow-up=8.8 yrs (Mass Male Aging)
- Ages 40-70
- Obesity status=significantly higher ED
- Physical activity=low ED risk (OR=0.5-0.8)
- Changes in smoking & alcohol=no effect

Derby CA, et al. Urology 56:302-306, 2000.

Randomized Trial-I

- Italian Study
- Randomized, 2-yrs!!!, n=110 obese (BMI ≥30)
- No diabetes, HTN, or dyslipidemia w/ED
- 21 or less on IIEF
- 55 men reduced calories, increase exercise

Esposito K, et al. JAMA 291:2978-2984, 2004.

Randomized Trial-II

- Age=43, BMI=36-37
- ED score=13-14 (range=1-25)
- hs-CRP=3.3-3.4 mg/L

Esposito K, et al. JAMA 291:2978-2984, 2004.

Randomized Trial-III

- BMI reduced 36.9 to 31.2
- Exercise increase from 48 to 195 min/week
- IIEF from 13 to 17 (17 men IIEF of 22 or more)
- BMI, Exercise, & hs-CRP associated w/IIEF
- hs-CRP=1.9 mg/L, HDL=48

Bottom Line=WOW!!!

Esposito K, et al. JAMA 291:2978-2984, 2004.

Moyad Secret=I Found the Magic Pill!

DRUG/MEDICAL CONDITION	SUGAR PILL IMPACT
E.D./F.S.D./BPH	25%
Hair Loss	42%
Hot Flashes (B. cohosh)	25-50%
Sleep (Insomnia)	25-50%
Weight Loss	6 pounds

#1 Magic Pill=Motivation (like smoking cessation)

Moyad MA. Urol Clin N Am, 2004

Placebo Effect

- Sildenafil=25% (women???)
- Apomorphine (40%)
- Vardenafil… (30-40%)
- Tadalafil (30%)

Bottom Line=Remember this???

Moyad MA. Urol Clin N Amer 29:11-22, 2002.

Lets Give Conventional Medicine More Opportunities?-I

- Provenge Example…just give us a chance

Moyad MA. Promoting Wellness, Ann Arbor Media Group, 2009.

Lets Give Conventional Medicine More Opportunities?-II

- ANEMIA DRUGS?
- ANGIOPLASTY
- ARTHROSCOPIC DEBRIDEMENT for OA
- ASPIRIN?
- BILATERAL LAPAROSCOPIC UTEROSACRAL NERVE ABLATION (LUNA) vs. Laparoscopy (no denervation) alone for CPP

Moyad MA. No BS Health Advice, Ann Arbor Media Group, 2009.

Lets Give Conventional Medicine More Opportunities?-III

- BLOOD PRESSURE DRUGS
- CHEMOTHERAPY FOR P. Ca..
- CHOLESTEROL-DRUGS (novel-torceptrapib)
- COLD REMEDIES
- COX-2 Inhibitors (Vioxx, 2-others…)
- CT SCANS…
- DIABETES (type II Medication)

Moyad MA. No BS Health Advice, Ann Arbor Media Group, 2009.