The Prudent Prescriber

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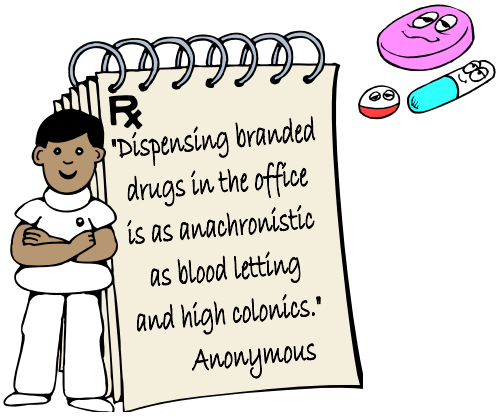


Low T: Time to Lower your Expectations Further

The first three of the seven long-awaited testosterone trials were published in the New England Journal of Medicine, February 18, 2016. The studies are disappointing. The results are disappointing. We are NOT any smarter about using testosterone in men older than 65 years, with low serum T, than we were before these studies.

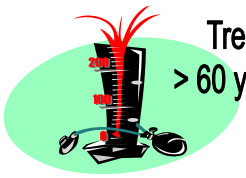
Clamored for by the Institute of Medicine and carried out and funded by the National Institutes of Health, these studies appear grossly underpowered. Investigators noted that relatively few (15%) of the more than 51,000 men who were screened to participate in the testosterone trials had low enough testosterone levels to qualify and only 790 men (1.5%) ultimately enrolled. Thus, the generalizability of these studies is modest, at best.

The findings are applicable only to men similar to the study subjects: older than 65, with serum testosterone levels less than 275ng/dL with associated sexual, physical or mood symptoms. Average age was 72 years, 90% of the participants were white, 72% had hypertension and 1/3 were diabetic.

Pharm Reps ≠ Rational Prescribing
(PR)  **(RP)**

CHF?
Think:
Ace
Aldactone
B-blocker
Dig
Diuretic

Avoid these expensive "me-too" drugs:
Intermezzo
Vimovo
Livalo
Pristiq
Viibyrd
Edarbi
Daliresp



Antibiotics do NOT help acute bronchitis

ß-blockers in post-MI save lives

Pill splitters save BIG

NOW AVAILABLE ON THE GENERIC MARQUEE

Lunesta→eszopiclone
Namenda→memantine
Axert→almotriptan
Prandimet→repaglinide/metformin
Jalyn→dutasteride/tamsulosin
Ortho Tri-Cyclen Lo→Tri-Lo-Marzia, Tri-Lo-Sprintec, & others

Results:
Testosterone treatment increased serum testosterone levels to the mid-normal range for men 19 to 40 years of age. The increase in testosterone levels was associated with increased sexual activity, as well as increased sexual desire and erectile function. The effect sizes were small for all of these outcomes (0.3 points on a 12 point scale at one year). The positive effects detumesced by the end of the first year. None of the effects on sexual function were as robust as those reported with use of phosphodiesterase type 5 inhibitors (e.g. Viagra,Cialis, Levitra). There were no statistical differences between testosterone and placebo groups on the six minute walk test or in the vitality trial. Three cases of prostate cancer developed in the testosterone treatment group and one in the placebo group. There was no difference between the two groups in urinary symptoms. No pattern of increased cardiovascular risk was identifiable, but the sample size was small.

My take:
These long-awaited studies are not revealing. There are no hard facts here. The call for bigger, more robust studies seems unrealistic in the face of the difficulties with coming up with even this small sample size. Do not hold your breath that the remaining four studies in this series will offer anything new. Testosterone manufacturers have successfully ramrodded a prime example of disease mongering. In this subset of men, testosterone supplementation is not a value-based intervention.

Ureteral stone? Thinking tamsulosin or nifedipine? Think again!

Two previous clinical reviews (Cochrane Renal Groups Specialized Registry, July 2012 and Seitz, Eur Urol 2009;56:455-471) that recommended medical expulsive therapy in adults with urethral colic suffered from collecting data from mostly small, poorly crafted studies.

Pickard et al in Lancet (July 25, 2015) cast these stones in a different light. This multicenter (24 UK NHS hospitals) controlled study randomized patients aged 18-65 with a single stone measuring 10 mm or smaller on CT to treatment with tamsulosin (378), nifedipine (379) or placebo (379). The primary outcome was spontaneous stone passage within four weeks of enrollment in the study. Participants self-administered tamsulosin 400µg, nifedipine 30mg or placebo orally, once daily until spontaneous passage occurred, requirement for intervention, or four weeks had elapsed.

Results:
80% of participants in the placebo group did not need further intervention by four weeks compared with the 81% of the tamsulosin group and 80% in the nifedipine group. No difference was noted between active treatment and placebo or between tamsulosin and nifedipine. Rates of additional stone passage by twelve weeks were also similar (7%, 6% and 7%) as was the meantime to passage - 14 days in each group. Pain ratings and use of pain medicine did not differ among groups. Serious adverse events occurred in three of the nifedipine patients (groin pain, diarrhea, vomiting, headache, chest pain, and dyspnea) and in one control patient (headache, dizziness, and abdominal pain).

My Take:
This is a large, well powered study. In my mind, Pickard’s work reverses the recommendation to utilize medical expulsive therapy. Utilizing nifedipine or tamsulosin in patients with urethral stones is not value based medicine.

Praxbind (PRAKS-bynd)

And finally, along comes the marketing genius of the decade! Boehringer Ingelheim wins the prize for developing the high priced antidote, idarucizumab (I dare you siz u mab) to their own anticoagulant Pradaxa (dabigatran). It feels like a grade B movie where the hero has to come up with a huge ransom to save metropolis from exsanguinating.

Idarucizumab

- Indicated when reversal of anticoagulant effects of Pradaxa is needed for emergency surgery or threatening/uncontrolled bleeding.
- Mechanism of action: as a monoclonal antibody fragment, binds to Pradaxa and rapidly neutralizes its effects.
- Administered as a 5g IV infusion
- Pradaxa therapy can be restarted in 24 hours.
- Pollack et al in NEJM 373(6):511, August 6, 2015, studied 90 adults with serious bleeding (n=51, median age 77) or requiring an urgent procedure (n=39, median age 76). For evaluable patients with bleeding (n=35), hemostasis was restored in 11.4 hours; for those having urgent procedures (n=36), intraoperative hemostasis was normal in 33 and mildly to moderately abnormal in 3. One thrombotic event occurred within 72 hours after idarucizumab administration in a patient in whom anticoagulants had not been reinitiated. This study suffers markedly from the lack of a control group.

My take:
Release of Praxbind does represent innovation and if subsequent better designed studies demonstrate effectiveness, idarucizumab will undoubtedly save lives. Although pricey at $3500 per dose, it is less expensive than prothrombin complex concentrate at $15,000 per dose.

You may access previous issues at http://www.rmhp.org/providers/prudent-prescriber.