Editorial Commentary

Changes in testosterone prescribing patterns after FDA warning

Soum D. Lokeshwar, Joshua Bitran, Ranjith Ramasamy

Department of Urology, University of Miami, Miami, FL, USA

Correspondence to: Ranjith Ramasamy. 1150 NW 14th St., Suite 309, Miami, FL 33136, USA. Email: ramasamy@miami.edu.

Comment on: Baillargeon J, Kuo YF, Westra JR, *et al.* Testosterone Prescribing in the United States, 2002-2016. JAMA 2018;320:200-2.

Submitted Mar 31, 2019. Accepted for publication Apr 12, 2019.

doi: 10.21037/tau.2019.04.03

View this article at: http://dx.doi.org/10.21037/tau.2019.04.03

Experts' summary

The research letter by Baillargeon *et al.* addresses the trends of testosterone prescription in the United States between 2002 and 2016. The investigators utilized data from Clinformatics Data Mart (CDM) and reported on the records of 9,962,538 men, ages 30 and above. The trends are reported as the total percentage of men who were prescribed testosterone therapy and the percentage of new testosterone users (no use in the prior year). Furthermore, the data was stratified for new users by age and region to account for testosterone prescription variation. The investigation found that testosterone use increased from 2002 to 2012 in both total and new users and then decreased from 2013 to 2016. The decrease was evident after stratification in all four regions and age groups of new users. By virtue of this study population from a commercial insurance database, the data is limited to employed men, and therefore not generalizable to elderly men.

Experts' comments

Building on the authors' previous study, which followed androgen prescribing trends from 2001 to 2011 (1), the investigators analyzed the prescription trends until 2016. Interestingly, the upward trend of testosterone prescribing reversed into a reduction of number of prescriptions from 2013 to 2016. The authors postulated that the increase in testosterone prescriptions from 2002 to 2012 was due to the direct-to-consumer marketing campaigns targeting middle-aged men and the increase of low-T centers (Baillargeon *et al.*). Additionally, the investigators suggested that the decrease in testosterone prescriptions in 2013 and 2014 coincided with two publications that reported increased incidence of myocardial infarction (MI) and stroke with testosterone therapy. The first, a retrospective national cohort study of male veterans in the Veterans Affairs system with low testosterone <300 ng/dL and significant medical comorbidities from 2005 to 2011, found the use of testosterone therapy was associated with an increased risk of mortality, MI, or ischemic stroke (2). Similarly, in 2014, a cohort study following 55,593 cases of initial testosterone therapy prescription, compared incidence rates of MI in the 90 days following initiation of treatment to 1 year prior. The study found that in younger men with pre-existing diagnosed heart disease and older men, the risk of MI following the initiation of testosterone therapy was substantially increased (3). Despite several limitations in these studies, the FDA added an advisory requiring a testosterone label change to include a warning on possible increased risk of MI and stroke in March of 2015 (4). The FDA advisory may have led many practitioners to exercise caution and hesitation when prescribing testosterone therapy.

It remains unclear if the decrease in number of testosterone prescriptions is due to previous overprescribing with a proper adjustment in the latter years, or if men with low testosterone are either not diagnosed or even worse—not treated. Although overprescription of testosterone therapy has been linked to cardiovascular risk, low testosterone has been found to be an independent risk factor for mortality (5). Practitioners that are nervous about cardiovascular risk with testosterone therapy should evaluate opportunity to prescribe more physiologic forms, such as short-acting nasal testosterone (Natesto) and medications that increase intratesticular production of testosterone such as human chorionic gonadotropin (hCG), and clomiphene citrate.

The decrease in testosterone prescribing may also signify a pendulum swing towards the middle ground, i.e., a shift away from overprescribing towards more balanced management practices. Still another possibility may involve a lack of accounting for all testosterone prescription due to compounding pharmacies and men paying cash for their prescriptions without insurance claims. Further studies should include a more comprehensive patient population to better understand overall testosterone therapy prescription risks and benefits.

Acknowledgments

None.

Footnote

Conflicts of Interest: Dr. Ranjith Ramasamy: Coloplast—consultant; Boston Scientific—investigator; Endo—investigator, advisory board; Aytu Biosciences—investigator, advisory board; Direx—investigator. The other authors have no conflicts of interest to declare.

Cite this article as: Lokeshwar SD, Bitran J, Ramasamy R. Changes in testosterone prescribing patterns after FDA warning. Transl Androl Urol 2019;8(Suppl 3):S287-S288. doi: 10.21037/tau.2019.04.03

References

1. Baillargeon J, Urban RJ, Ottenbacher KJ, et al. Trends in androgen prescribing in the United States, 2001 to 2011. JAMA Intern Med 2013;173:1465-6.
2. Vigen R, O'Donnell CI, Barón AE, et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. JAMA 2013;310:1829-36.
3. Finkle WD, Greenland S, Ridgeway GK, et al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. PLoS One 2014;9:e85805.
4. Seftel AD. Re: Testosterone Products: Drug Safety Communication - FDA Cautions about Using Testosterone Products for Low Testosterone due to Aging; Requires Labeling Change to Inform of Possible Increased Risk of Heart Attack and Stroke. J Urol 2015;194:759-60.
5. Shores MM, Matsumoto AM. Testosterone, aging and survival: biomarker or deficiency. Curr Opin Endocrinol Diabetes Obes 2014;21:209-16.

