alterations in the intrauterine environment can lead to permanent changes in the number, structure, and even function of different types of cells, tissues, and organs, increasing susceptibility to any diseases throughout the course of a person's life [1]. There is evidence indicating that some deleterious maternal conditions could be the trigger for programming mechanisms that explain the development of some diseases during the life of offspring [2–4].

However, there is increasing focus on the role of fathers as new evidence highlights the paternal contribution to the health of the next generation. In this context, Borges et al. [5] demonstrate that the men with poor lifestyle habits such as cigarette smoking and drinking have poor reproductive outcomes (ie, ability to fertilize). Soubry [6] coined the term *Paternal Origins of Health and Disease* to make the point that obesity, poor exercise, smoking, and excessive drinking habits of fathers can negatively impact the development of the paternal germline. In the same vein, our group has demonstrated the positive effect of a father's diet rich in antioxidants on pregnancy outcomes for women who have suffered recurrent gestational loss [7,8].

Information like this is of great relevance because the number of individuals suffering from noncommunicable diseases is increasing worldwide, and lifestyle can influence the occurrence of these types of illness. The World Health Organization [9] reported an average intake of 6.2 l of pure alcohol by individuals aged >15 yr, which equates to a daily intake of approximately 13.5 g/d of pure alcohol. On a global basis, 23% of adults are physically inactive and 11% of adult men are obese.

Therefore, it is not illogical to assume that individuals with excessive alcohol intake or weight, or those who smoke and do not exercise frequently enough could experience fertility problems in the future, or could have negative consequences for their children's health. It is time to act, and this evidence provides further motivation to change unhealthy lifestyle habits.

Conflict of interest: The authors have nothing to disclose.

References

[1] Musumeci G, Castrogiovanni P, Trovato FM, Parenti R, Szychlinska MA, Imbesi R. Pregnancy, embryo-fetal development and nutrition: physiology around fetal programming. J Histol Histopathol 2015;2:1.
[2] Triunfo S, Lanzone A. Impact of maternal under nutrition on obstetric outcomes. J Endocrinol Invest 2015;38:31–8.
[3] Langley-Evans SC. Nutrition in early life and the programming of adult disease: a review. J Hum Nutr Diet 2015;28(Suppl 1):1–14.
[4] Adamo KB, Ferraro ZM, Brett KE. Can we modify the intrauterine environment to halt the intergenerational cycle of obesity? Int J Environ Res Public Health 2012;9:1263–307.
[5] Borges Jr E, Braga DPAF, Provenza RR, Figueira RCS, Iaconelli Jr A, Setti AS. Paternal lifestyle factors in relation to semen quality and in vitro reproductive outcomes. Andrologia 2018;50:e13090.
[6] Soubry A. POHaD: why we should study future fathers. Environ Epigenet 2018;4:dvy007.
[7] Gil-Villa AM, Cardona-Maya W, Agarwal A, Sharma R, Cadavid A. Assessment of sperm factors possibly involved in early recurrent pregnancy loss. Fertil Steril 2010;94:1465–72.
[8] Gil-Villa AM, Cardona-Maya W, Agarwal A, Sharma R, Cadavid A. Role of male factor in early recurrent embryo loss: do antioxidants have any effect? Fertil Steril 2009;92:565–71.
[9] World Health Organization. Global status report on noncommunicable diseases. 2014. www.who.int/nmh/publications/ncd-status-report-2014/en

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Re: A Prospective Randomised Placebo-controlled Study of the Impact of Dutasteride/Tamsulosin Combination Therapy on Sexual Function Domains in Sexually Active Men with Lower Urinary Tract Symptoms (LUTS) Secondary to Benign Prostatic Hyperplasia (BPH)

Roehrborn CG, Manyak MJ, Palacios-Moreno JM, et al

BJU Int 2018;121:647–58

Experts' summary:

This is the first randomised clinical trial (double-blind and placebo-controlled) to prospectively assess the effects of dutasteride and tamsulosin (DUT-TAM) combination therapy on subdomains of sexual function in men with benign prostatic hyperplasia (BPH) having lower urinary tract symptoms (LUTS) and prostate volume of ≥30 cm^3. The authors used the Male Sexual Health Questionnaire (MSHQ) to assess three core domains (erection, ejaculation and satisfaction) of male sexual function at baseline and 1, 3, 6, 9, and 12 mo; higher scores indicate better sexual function.

The intent-to-treat population included 489 patients (243 DUT-TAM and 246 placebo). A significant decrease (worsening) was observed with DUT-TAM therapy versus placebo on the total MSHQ score (-8.7 vs - 0.7;SE: 0.81, 0.78; $p < 0.001$) and the ejaculation and satisfaction domains, but not the erection domain (-1.0 vs -0.5; SE: 0.19, 0.19; $p = 0.091$).

The most common drug-related adverse events (AEs) were those in the reproductive system and breast disorder

categories, which were higher in the DUT-TAM than in the placebo group (33% vs 14%). Regarding reproductive system AEs, the number of unresolved cases of erectile dysfunction (ED) after 18 mo was remarkably similar in both groups. By contrast, 6 mo after cessation of treatment, five and 23 cases of ejaculation dysfunction (EjD) remained unresolved in the placebo and DUT-TAM groups, respectively.

Experts' comments:

This article gives an interesting insight into the management of one of the most common clinical scenarios in urology. 5α-Reductase inhibitors (5ARIs) such as finasteride and dutasteride have been consistently blamed for causing sexual dysfunction such as decreased libido, ED, and EjD in many animal and human studies [1].

This study used three MSHQ subdomains and concluded that the combination therapy lead to only EjD and not ED. The significant EjD caused by the combined therapy in this study could be due to the additive effects of both tamsulosin (α-blocker) causing retrograde ejaculation and dutasteride causing shrinkage of the prostate by at least 25–30% in size [2]. The shrinkage in prostate size could lead to a decrease in prostatic secretions, thereby reducing the ejaculate volume and causing subsequent EjD in some men. This could also explain the significant number of unresolved cases of EjD after treatment cessation.

The most interesting outcome of the study was that there was no significant difference in erectile domain between the groups. So why is it a general impression that the DUT-TAM combination causes ED? In our opinion, there are two possible answers to this question. First, most urologists do not ask about erectile function before starting LUTS treatment, although it is well known that ED is prevalent and underdiagnosed in patients consulting for LUTS [3]. Patients become aware of their sexual problems after the treatment is initiated or when the doctor questions them about details of their sexuality. Second, some "nocebo effect" may be involved. In fact, "counselling" on the possible negative impact on sexual function affects AE reporting and can cause up to three times as many men to report sexual dysfunction [4].

Libido alterations in this study were only referred to as AEs, even though there are four questions about sexual desire in the questionnaire, so it is possible that this aspect of sexual dysfunction was under-reported in the article. In fact, it seems plausible that the effect of dutasteride on testosterone and dihydrotestosterone metabolism could have led to a negative impact on sexual desire. A meta-analysis by Corona et al. [5] highlighted that 5ARIs were associated with a greater risk of hypoactive sexual desire (odds ratio [OR] 1.54, 95% confidence interval [CI] 1.29–1.82; $p < 0.0001$) and ED (OR 1.47, 95% CI 1.29–1.68; $p < 0.0001$).

Most studies assessing sexual function have used the International Index of Erectile Function and its subdomains. Only a few have used the MSHQ total score, but we should appreciate the authors' use of the subdomains of the MSHQ.

The major limitation of the study was, of course, the exclusion of tamsulosin-only and dutasteride-only groups to better define the role of each drug in the different sexual function domains and to see if there was any additive effect of the combination.

This interesting study sheds light on this controversial topic that serves as an aid for urologists to better understand the sexual effects of common treatments for BPH/LUTS and the appropriate counselling that should be provided to this subset of patients.

Conflicts of interest: The authors have nothing to disclose.

References

[1] Traish AM, Mulgaonkar A, Giordano N. The dark side of 5α-reductase inhibitors' therapy: sexual dysfunction, high Gleason grade prostate cancer and depression. Korean J Urol 2014;55:367–79.

[2] Amory JK, Wang C, Swerdloff RS, et al. The effect of 5α-reductase inhibition with dutasteride and finasteride on semen parameters and serum hormones in healthy men. J Clin Endocrinol Metab 2007;92:1659–65.

[3] Seftel A, Rosen R, Kuritzky L. Physician perceptions of sexual dysfunction related to benign prostatic hyperplasia (BPH) symptoms and sexual side effects related to BPH medications. Int J Impot Res 2007;19:386–92.

[4] Mondaini N, Gontero P, Giubilei G, et al. Finasteride 5 mg and sexual side effects: how many of these are related to a nocebo phenomenon? J Sex Med 2007;4:1708–12.

[5] Corona G, Tirabassi G, Santi D, et al. Sexual dysfunction in subjects treated with inhibitors of 5α-reductase for benign prostatic hyperplasia: a comprehensive review and meta-analysis. Andrology 2017;5:671–8.

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Re: Mechanical Failure Rates of Artificial Urinary Sphincter Components: Is the 3.5-cm Urethral Cuff at Higher Risk?

Loh-Doyle JC, Hartman N, Nazemi A, Ginsberg D, Boyd S

Neurourol Urodyn. In press. https://doi.org/10.1002/nau.23825

Expert's summary:

The 3.5-cm cuff was introduced in 2010 to theoretically meet the needs of surgeons who encountered smaller urethras. The authors demonstrated that a 3.5-cm cuff is more prone to mechanical failure and reoperation. Despite these higher complication rates, the authors conclude that