The Aging Male

ISSN: (Print) (Online) Journal homepage: informahealthcare.com/journals/itam20

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To cite this article: Dr Nisanth Puliyath & Dr Venugopalan AV (2024) Navigating the unregulated terrain of testosterone boosters: a growing concern in men's health, The Aging Male, 27:1, 2312176, DOI: 10.1080/13685538.2024.2312176

To link to this article: https://doi.org/10.1080/13685538.2024.2312176

Published online: 02 Feb 2024.

THE AGING MALE
2024, VOL. 27, NO. 1, 2312176
https://doi.org/10.1080/13685538.2024.2312176

Taylor & Francis
Taylor & Francis Group

LETTER TO THE EDITOR

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Navigating the unregulated terrain of testosterone boosters: a growing concern in men's health

Dear Editor,

Recent times have witnessed a surge in interest in various fields related to Testosterone replacement therapy (TRT). Both the American urological association and the society for endocrinology endorses the use of testosterone for patients exhibiting clear signs of hypogonadism [1,2]. This endorsement is substantiated by a substantial body of evidence highlighting TRT's positive impact on erectile function, muscle mass, strength, bone health, fatty tissue, and metabolic control [3]. As a result of this TRT usage has surged in recent times because of its expanding indications and with all known evidence from long-term studies of TRT on male hypogonadism, prescribing of TRT has become more permissive. The usage is expected to increase even more following the recent TRAVERSE study, which has demonstrated the cardiovascular safety of TRT [4] alleviating side effect concerns.

But the recent year has witnessed an increase in marketing and usage of "alternative and natural ways" of enhancing testosterone (T) levels, in the form of so-called testosterone boosters (T-boosters) or testosterone enhancers. T-boosters are plant-based food supplements marketed for their proposed benefit of increasing serum levels of testosterone, enhancing the testosterone effects, or improving the symptoms of hypogonadism.

They are mainly marketed *via* internet-based platforms and their easy availability without prescriptions, lower cost (compared to standard TRT), and absence of any regulations make it a booming industry. According to recent data, the global testosterone booster supplements market was estimated at US$ 72.8 million in 2022 and is anticipated to grow to US$ 144.2 million in 2033 [5]. These products are especially taken by athletes or bodybuilders for their perceived benefit of performance enhancement. As there is a renewed interest in our society regarding fitness and supplements in recent times, fuelled by the "fitness gurus" or health & nutrition influencers in various social media platforms, the T-booster usage only seems to hike in the future. A mere search in popular social media platforms like Instagram or YouTube reveals thousands of such videos by various influencers, unmoderated health information available at the fingertips of everyone with attached easy buying links. There seems to be an artificially created awareness and need because of these influencer videos, sponsored by T-booster supplement manufacturers in many cases.

So, we would like to write this letter to the editor to draw his attention to this important public health issue in men's health which has wider implications, yet neglected by mainstream medicine and remains unregulated. There is a proliferation of food supplements claiming to boost testosterone levels on e-commerce sites. These supplements, predominantly feature a variety of ingredients like *Tribulus terrestris* [6], fenugreek, zinc [7], maca [8], melatonin, ashwagandha [9], tongkat ali extract, horny goat weed, saw palmetto extract, ginseng root extract, *Ginkgo biloba* leaf extract [10], Boron, nettle extract to name a few. T-boosters remain unregulated by the FDA and are marketed as food supplements rather than medications. A study on these online products reported that nearly 30% of product reviews reported improvements in "energy" levels after consumption [11].

Tribulus terrestris (*Zygophillacae*), a common component in many T-boosters, contains active metabolites believed to raise T levels, yet the evidence remains inconclusive [6]. The role of Tribulus terrestris as a T-booster seems to be controversial as there are some studies showing benefits with testosterone level increase along with improving the sexual function of patients who suffered from erectile dysfunction with partial androgen deficiency [12,13], which are in contradiction to the studies finding no direct or indirect androgen increasing properties with this herb [14]. Ashwagandha (*Withania somnifera)*, on the other hand, has shown some promise by increasing testosterone levels by 15% and an 18% increase in DHEA-S levels compared to the placebo, but its effects on cortisol and estradiol are inconclusive [9]. There appears to be a link between zinc deficiency and hypogonadism and zinc supplementation might reverse this condition. However, there's no clear evidence of testosterone increase in healthy individuals due to zinc supplementation, and excess zinc intake can lead to health complications [7]. Maca *(Lepídium meyenií*) is a Peruvian herb, a widely used ingredient of T-boosters, and is credited with potential benefits for erectile dysfunction, physical performance, and sperm count. Its mechanism of action remains elusive, but its positive effects in rat studies are noted. Studies show that it may increase sperm count but doesn't increase T levels [8]. The Ginkgo monotherapy failed to increase testosterone levels, but showed a slight increase in T levels, when "combined with exercise" [10].

While some studies have suggested potential increases in serum T levels with these supplements, many studies

underscore the inconsistency in results and a lack of methodological rigor across many of these studies. Additionally, concerns about serious adverse effects, such as hepatotoxicity, severe neurological disorders, and renal failure after high-dose consumption, are also reported [6]. Consequently, the existing body of literature does not offer substantial support for the use of these products. The non-standardization of the ingredients, wide variation of both contents and their composition, absence of any safety warning or dosage limit, and potential interaction with other drugs, all complicate the dark realm of T-boosters. Since this is an over-the-counter product, these products are many times consumed by healthy people who may not need a testosterone supplementation in the first place. They may be consumed beyond the approved indications of TRT, like fitness and stamina enhancement, sexual wellness, and overall general health booster. Since these topics are not well covered in modern medical practice in depth, there seems to be a lacuna of knowledge among the care providers regarding these products. Considering the wide andrological and health economics importance, there is a need for wider awareness among all the health professionals involved in men's health care.

All these matters bring some important questions too. Like, if they may be associated with harmful side effects with not completely proven benefit, shouldn't T-boosters be regulated more stringently by our regulatory bodies, even if they disguise themselves as "food supplements"? We need to conduct more rigorously done studies to evaluate the perceived benefits of such products and need to standardize their dose and ingredient levels. Since conditions like partial androgen deficiency of aging male (PADAM) involve a gradual decline of testosterone, with a mild decrease in the initial stages, the potential clinical utility of T-boosters in such conditions can be explored. And more importantly, if we are talking about "the best natural ways of boosting testosterone", then the more proven, yet simple-to-do methods like stress reduction, getting quality sleep [15], regular exercises, eating a balanced diet, weight reduction, quitting smoking, and alcohol are the ways to go. This knowledge should be imparted to the targeted population amidst all these marketing tactics, as they need to know there exists a "proven yet side-effect free way" with not spending this much for boosting testosterone. There also needs to be guidelines for moderating the health content of social media videos on the internet with adding disclaimers like the COVID-19 times. There is also a chance that these testosterone boosters might persuade deserving patients away from their recommended TRT, as the gullible patients might think that this cheaper alternative might work. There is a need for increased awareness among patients and clinicians alike regarding T-boosters. The utility of these products warrants active research as the potential benefits are interesting. One such area of future research is their potential application to the perimenopausal women. The application of transdermal testosterone products are effective in postmenopausal women with low sexual desire causing distress, making this an interesting arena to explore for T-booster supplements for any perceived benefits in future studies [16].

While TRT remains a well-supported treatment for male T deficiency, the evidence for the efficacy and safety of over-the-counter testosterone-boosting supplements is lacking, with concerns about adverse effects. Caution and informed decision-making are advised when considering these products.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

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Received 27 September 2023; Revised 11 December 2023; Accepted 26 January 2024; Published online 27 January 2024

https://doi.org/10.1080/13685538.2024.2312176