

Risk Associated with Supplements and Enhancing Drugs: Letter to the Editor

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Respected Sir,

The use of dietary supplements is widespread in the general population, in athletes and recreational exercisers, and in military personnel. A wide array of supplements is available. DSs seldom prescribed to critically ill patients as well. In US, there are an estimated three million anabolic-androgenic users of whom 60% are non-competitive recreational bodybuilders or non-athletes, who use these drugs for cosmetic purposes [1]. Approximately 70% of these supplements were sport and protein beverages or powder. It was recognized over a decade ago that some 20% of nutritional supplements sold in Europe and the USA contained anabolic steroids [2]. Anabolic steroid abuse could lead to reduced fertility and increased cardiovascular diseases [3]. The most likely cause of the patient's systemic and metabolic disturbances is hypercalcemia. As previously reported, constipation, anorexia, nausea and vomiting are often the prominent symptoms of hypercalcemia [4]. Indeed, one fourth of opiate users admitted to treatment centers acknowledged an earlier use of steroids [5]. An increased health awareness among athletes and the public will favor the global sports nutrition market which is predicted to have an annual growth rate of 9% from 2013 to 2019, to an estimated value of USD 37.7 billion in 2019 [6]. In addition to supplementation timing, the optimal dosage also needs to be considered [7]. It was observed that a dose higher than 300 mg/kg of sodium bicarbonate likely causes gastrointestinal discomfort [8]. Creatine supplementation is an established ergogenic aid in sports and is now claimed to have therapeutic applications in a variety of diseases [9]. A risk for acute and potentially chronic kidney injury among young men abusing anabolic steroids and using excessive amounts of nutritional supplements already

reported [10]. Reported cases of herbals and DS-induced liver injury are increasing worldwide. Regulation of herbal products may vary between different countries. In the European Union, the concepts of traditional herbal medicines and traditional plant food supplements are defined under different legal frameworks [11]. Herbals and dietary supplements induced liver injury found in Asian countries where there is a widespread consumption of HDS, 73% in Korea, 71% in Singapore, and 40% in China [12]. The 17- α -alkylation modification allows steroids to be taken orally, but the slower clearance in the liver makes them more hepatotoxic [13]. Data from the US suggest that 1-3 % of the inhabitants use anabolic steroids. The lifetime prevalence of anabolic androgenic steroids use in the US was estimated in a recent study with about 3-4 million [14]. Again, case reports revealed the connection between myocardial infarction, myocardial hypertrophy and hypertension with anabolic androgenic steroids abuse [15]. Major mood disorders, aggressive behavior, dependence syndrome, or cognitive effects also reported to a significant extent [16]. Caffeine is perhaps the most common pre-workout stimulant consumed by bodybuilders. Numerous studies support the use of caffeine to improve performance during endurance training [17, 18]. Many mechanisms have been suggested in relation to caffeine toxicity, which primarily affects the cardiovascular system [19]. However, at present the evidence base exploring both caffeine habituation and withdrawal strategies in athletes is surprisingly small. Accordingly, despite the prevalence of caffeine use within athletic populations, formulating evidence-led guidelines is difficult [20]. Potential for diarrhea, nausea, abdominal cramps, and other gastrointestinal disturbances

with vitamin C intakes of more than 2,000 mg/day in adults; increased risk of hemorrhagic effects with vitamin E intakes of more than 1,500 IU/day (natural form) or 1,100 IU/day (synthetic form) in adults; nausea, heartburn, and other side effects with coenzyme Q10 [21]. Some 30000 supplements are commercially-available in the USA [22]. Recent research also shows that athletes are willing to take supplements based on personal recommendation without gathering reliable information about the substances, often obtaining them directly from retailers and internet sites. Adolescents are more willing to take supplements obediently if they are informed by their parents/guardians, as opposed to by coaches or resulting from published research [23]. Excess intake of vitamin C can be harmful as well as in combination with iron, which may cause damage to the gastrointestinal tract and initiate or aggravate symptoms associated with chronic GI disorders [24, 25]. Cobalt produces similar effects to hypoxia and results in enhanced erythropoiesis, thus in improved sport performance but such practice may be harmful [26]. Whilst the controversial natural stimulant, ephedrine, has a threshold (concentration in the urine exceeds 10 µg/ml) for consideration for doping, the serious harm, which may be caused by ephedrine is well documented [27, 28]. Some supplements have even been implicated as the cause of death and disability when used improperly [29]. 75% athlete reported using calorie replacement products including drinks, bars, and powders [30]. Similarly, the use of vitamins and multivitamins ranges from 26 to 82% among athletes. The use of multivitamins and vitamin C is higher than 50% and 80%, respectively [31, 32]. The reasons these athletes use vitamins are primarily to stay healthy and to prevent illnesses during the game season [33]. The sudden heart attack death of former baseball star Ken Caminiti, 41, highlights the potential link between substance abuse among pro athletes and its dangerous effects on health, according to experts [34]. Bodybuilding brothers Mike and Ray Mentzer of Redondo Beach, California, were both plagued with health problems in their late '40s after long careers. Ray officially died of kidney failure, and Mike's death was heart-related [35]. Elite bodybuilder Rich Piana has died, police later revealed they found bottles of testosterone and white powder in the house [36]. High testosterone dosages appeared to be protective of erectile function during use, de novo symptoms such as decreased libido and erectile

function occurred more frequently after discontinuing testosterone, particularly among those using more frequently and for longer durations [37]. Testosterone booster products obtained from trusted sources and administered as per the recommendations of the manufacturer may still present some health risks [38]. Former anabolic androgenic steroids abusers exhibited significantly lower plasma testosterone levels and higher frequencies of symptoms suggestive of hypogonadism than healthy control participants years after anabolic androgenic steroids cessation [39]. Unfortunately, since most men begin anabolic androgenic steroids at a young age and are presumed to obtain the medication from illicit sources, they are not educated regarding the possible negative outcomes that come with their use [40]. In addition to damage to other organs, a diverse range of nephrotoxicities have been reported with dietary supplements. A case report reveals acute tubular necrosis with vacuolization, acute interstitial nephritis, and secondary membranous nephropathy, consistent with an NSAID-like nephropathy [41]. The endocrine effects of anabolic androgenic steroids abuse are well established and commonly include testicular atrophy, decreased fertility, and gynecomastia. Additional adverse effects associated with AASs include changes in blood lipid levels (increase in LDL and decrease in HDL) and neuropsychiatric disturbances [42]. Ephedra and ephedrine for weight loss and athletic performance enhancement is well-known. An association between short-term use of ephedrine, ephedrine plus caffeine, or dietary supplements that contain ephedra with or without herbs containing caffeine and a statistically significant increase in short-term weight loss is established. But that they are associated with increased rates of side-effects. These conclusions reflected the limited evidence available and are likely to be reliable [43]. Weight Loss regardless of its severity could improve anthropometric indicators, although body composition is more favorable following a slow weight loss [44]. However, several sport nutrition experts indicated that some athletes may be at risk for a vitamin deficiency, such as those in weight-control sports and those who for one reason or another do not eat a well-balanced diet. Vitamin supplementation, particularly when limited to 100% of the RDA (Recommended Dietary Allowance) for each vitamin, is generally regarded as safe [45]. The worldwide use of DS by athletes warrants attention and more research as there is a number

of commonly used supplements that have not been thoroughly investigated. Furthermore, the intake of more than one supplement (polypharmacy) in high doses and for long periods of time poses serious concerns regarding their safety [46]. Although adulteration with drugs is by definition fraudulent, the inclusion of heavy metals could be either intentional for alleged medicinal purposes or accidental. Because they are not regulated as medicines and are freely available to everyone, serious safety concerns might be associated with these herbal medicines [47]. Contamination of soil, water, and air directly leads to contamination of plants and herbal preparations, and high levels of heavy metals such as lead, mercury, and arsenic, which have been observed in some traditional Chinese medicines and Indian herbal medicine preparations. Lead intake from TCM in this study was 3-4000 times higher than the recommended amount [48]. The National Collegiate Athletic Association (NCAA) prohibits the use of anabolic steroids by athletes and lists this class of drugs as banned substances. First anabolic steroids to be used as a doping agent by professional athletes in the 1960s. It was banned from the Olympics by the IOC (International Olympic Committee) in 1974 [49]. Diet can significantly influence athletic performance, but recent research developments have substantially changed our understanding of sport and exercise nutrition. Athletes adopt various nutritional strategies in training and competition in the pursuit of success [50]. The need for more research and understanding of the reasons and educational sources of these athletes in order to form the basis for educational programs on dietary supplementation and to reduce the chances of positive doping and disqualification from competition.

REFERENCES

- [1] M-P Sharma, A Chalmers; Anaesthetic implications of performance-enhancing drugs, *BJA Education*, Volume 16, Issue 7, 1 July 2016, Pages 247–251, <https://doi.org/10.1093/bjaed/mkv055>
- [2] Martin SJ, Sherley M, McLeod M. Adverse effects of sports supplements in men. *Aust Prescr*. 2018;41(1):10-13.
- [3] Samaha AA, Nasser-Eddine W, Shatila E, Haddad JJ, Wazne J, Eid AH. Multi-organ damage induced by anabolic steroid supplements: a case report and literature review. *J Med Case Rep*. 2008;2:340. Published 2008 Oct 31. doi:10.1186/1752-1947-2-340
- [4] Goldfarb S, Agus ZS. Mechanism of the polyuria of hypercalcemia. *Am J Nephrol*. 1984;4:69–76.
- [5] Kanayama G, Cohane GH, Weiss RD, Pope HG. Past anabolic-androgenic steroid use among men admitted for substance abuse treatment: an underrecognized problem? *J Clin Psychiatry*. 2003;64:156–160.
- [6] Naderi A, de Oliveira EP, Ziegenfuss TN, Willems MT. Timing, Optimal Dose and Intake Duration of Dietary Supplements with Evidence-Based Use in Sports Nutrition. *J Exerc Nutrition Biochem*. 2016;20(4):1-12.
- [7] Kakigi R, Yoshihara T, Ozaki H, Ogura Y, Ichinoseki-Sekine N, Kobayashi H, Naito H. Whey protein intake after resistance exercise activates mTOR signaling in a dose-dependent manner in human skeletal muscle. *Eur J Appl Physiol*. 2014; 114:735–42. doi:10.1007/s00421-013-2812-7.
- [8] McNaughton LR. Bicarbonate ingestion: effects of dosage on 60s cycle ergometry. *J Sports Sci*. 1992; 10:415–23. doi:10.1080/02640419208729940.
- [9] Souza RA, Miranda H, Xavier M, et al. Effects of high-dose creatine supplementation on kidney and liver responses in sedentary and exercised rats. *J Sports Sci Med*. 2009;8(4):672-81. Published 2009 Dec 1.
- [10] Almkhatar SE, Abbas AA, Muhealdeen DN, Hughson MD. Acute kidney injury associated with androgenic steroids and nutritional supplements in body builders (†). *Clin Kidney J*. 2015;8(4):415-9.
- [11] Serafini M., Stanzione A., Foddai S., Anton R., Delmulle L. The European role on traditional herbal medicinal products and traditional plant food supplements. *J. Clin. Gastroenterol*. 2012; 46: S93–S94. doi: 10.1097/MCG.0b013e318266b08f.
- [12] García-Cortés M, Robles-Díaz M, Ortega-Alonso A, Medina-Caliz I, Andrade RJ. Hepatotoxicity by Dietary Supplements: A Tabular Listing and Clinical Characteristics. *Int J Mol Sci*. 2016;17(4):537. Published 2016 Apr 9. doi:10.3390/ijms17040537
- [13] Niedfeldt MW. Anabolic Steroid Effect on the Liver. *Curr Sports Med Rep*. 2018 Mar;17(3):97-102. doi:10.1249/JSR.0000000000000467. Review. PubMed PMID: 29521706.
- [14] Joseph JF, Parr MK. Synthetic androgens as designer supplements. *CurrNeuropharmacol*. 2015;13(1):89-100.
- [15] Martinez-Quintana E., Saiz-Udaeta B., Marrero-Negrin N., Lopez-MA(c)rida X., Rodriguez-Gonzalez F., Nieto-Lago V. Androgenic anabolic steroid, cocaine and amphetamine abuse and adverse cardiovascular

- effects. *Int. J. Endocrinol. Metab.* 2013;11(4): e8755. doi: 10.5812/ijem.8755.
- [16] Clark A.S., Henderson L.P. Behavioral and physiological responses to anabolic-androgenic steroids. *Neurosci. Biobehav. Rev.* 2003;27(5):413–436. doi:10.1016/S0149-7634(03)00064-2.
- [17] Ivy JL, Kammer L, Ding Z, Wang B, Bernard JR, Liao YH, Hwang J. Improved cycling time-trial performance after ingestion of a caffeine energy drink. *Int J Sport NutrExercMetab.* 2009;19:61–78.
- [18] McNaughton LR, Lovell RJ, Siegler J, Midgley AW, Moore L, Bentley DJ. The effects of caffeine ingestion on time trial cycling performance. *Int J Sports Physiol Perform.* 2008;3:157–163.
- [19] Cappelletti S, Piacentino D, Sani G, Aromatario M. Caffeine: cognitive and physical performance enhancer or psychoactive drug? *CurrNeuropharmacol.* 2015 Jan;13(1):71-88. doi: 10.2174/1570159X13666141210215655. Review. Erratum in: *CurrNeuropharmacol.* 2015;13(4):554. Daria, Piacentino [corrected to Piacentino, Daria]. PubMed PMID: 26074744; PubMed Central PMCID: PMC4462044.
- [20] Pickering C, Kiely J. What Should We Do About Habitual Caffeine Use in Athletes? *Sports Med.* 2018 Sep 1. doi: 10.1007/s40279-018-0980-7. [Epub ahead of print] PubMed PMID: 30173351.
- [21] Web National Institute of Health (NIH). Dietary Supplements for Exercise and Athletic Performance. Available From: <https://ods.od.nih.gov/factsheets/ExerciseAndAthleticPerformance-HealthProfessional/>
- [22] Petróczi A, Naughton DP. Supplement use in sport: is there a potentially dangerous incongruence between rationale and practice?. *J Occup Med Toxicol.* 2007;2:4. Published 2007 May 29. doi:10.1186/1745-6673-2-4
- [23] Bartee RT, Grandjean B, Dunn MS, Perko MA, Eddy JM, Wang MQ. Predictors of dietary supplement use among adolescent athletes. *Pediatric Exerc Sci.* 2004;16:250–264.
- [24] Fisher AEO, Naughton DP. Iron supplements: the quick fix with long-term consequences. *Nutr J.* 2004;3:1475–2891. doi:10.1186/1475-2891-3-2.
- [25] Wroblewski K. Can the administration of large doses of vitamin C have a harmful effect? *Pol MerkuriuszLek.* 2005;19:600–603.
- [26] Lippi G, Franchini M, Guidi GC. Blood doping by cobalt. Should we measure cobalt in athletes? *J Occupational Med Toxicol.* 2006;1:18. doi: 10.1186/1745-6673-1-18. doi:10.1186/1745-6673-1-18.
- [27] Haller CA, Meier KH, Olson KR. Seizures reported in association with use of dietary supplements. *Clin Toxicol (Phila)* 2005;43:23–30. doi: 10.1081/CLT-44771.
- [28] Shekelle PG, Hardy ML, Morton SC, Maglione M, Mojica WA, Suttorp MJ, Rhodes SL, Jungvig L, Gagné J. Efficacy and Safety of Ephedra and Ephedrine for Weight Loss and Athletic Performance. A Meta-analysis. *JAMA.* 2003;289:1537–1545. doi:10.1001/ jama.289.12.1537.
- [29] Dunn MS, Eddy JM, Wang MQ, Nagy S, Perko MA, Bartee RT. The influence of significant others on attitudes, subjective norms and intentions regarding dietary supplement use among adolescent athletes. *Adolescence-Sandiego.* 2001;36(143):583–592.
- [30] Molinero O, Márquez S. Use of nutritional supplements in sports: risks, knowledge, and behavioural-related factors. *Nutrición Hospitalaria.* 2009;24(2):128–134.
- [31] Baylis A, Cameron-Smith D, Burke LM. Inadvertent doping through supplement use by athletes: assessment and management of the risk in Australia. *International Journal of Sport Nutrition.* 2001;11(3):365–383
- [32] Burns RD, Schiller MR, Merrick MA, Wolf KN. Intercollegiate student athlete use of nutritional supplements and the role of athletic trainers and dietitians in nutrition counseling. *Journal of the American Dietetic Association.* 2004;104(2):246–249.
- [33] Azizi M, Mali AD, Tabari E. Study of prevalence of supplement use and knowledge of men national team rowers about doping and side effects. *World Applied Sciences Journal.* 2012;17(6):724–728.
- [34] Caminiti's Death Puts Spotlight on Steroids. *Web Health Day MONDAY, Oct. 11, 2004*
- [35] Celebrity Bodybuilders Who Died from Steroid Use. *Web Supplement Source Canada.* Available From: <http://supplementsource.ca/v/celebritybodybuilders/>
- [36] Lake E. Steroid-using celeb bodybuilder dies two weeks after falling into coma. *The Sun* August 25, 2017
- [37] Armstrong JM, Avant RA, Charchenko CM, et al. Impact of anabolic androgenic steroids on sexual function. *TranslAndrol Urol.* 2018;7(3):483-489.
- [38] Almainan AA. Effect of testosterone boosters on body functions: Case report. *Int J Health Sci (Qassim).* 2018;12(2):86-90.
- [39] Rasmussen JJ, Selmer C, Østergren PB, et al. Former Abusers of Anabolic Androgenic Steroids Exhibit Decreased Testosterone Levels and Hypogonadal Symptoms Years after Cessation: A Case-Control Study. *PLoS One.*

- 2016;11(8):e0161208. Published 2016 Aug 17. doi:10.1371/journal.pone.0161208
- [40] Kovac JR, Scovell J, Ramasamy R, et al. Men regret anabolic steroid use due to a lack of comprehension regarding the consequences on future fertility. *Andrologia*. 2014;47(8):872-8.
- [41] Koraihy FM, Moeckel GW, Geller DS. A case of severe nephrotoxicity associated with long-term dietary supplement use [published online ahead of print, 2017 Aug 2]. *Clin Nephrol*. 2017;5:42–47. doi:10.5414/CNCS109180
- [42] Herlitz LC, Markowitz GS, Farris AB, et al. Development of focal segmental glomerulosclerosis after anabolic steroid abuse. *J Am Soc Nephrol*. 2010;21(1):163-72.
- [43] Shekelle P, Hardy ML, Morton SC, et al. Ephedra and Ephedrine for Weight Loss and Athletic Performance Enhancement: Clinical Efficacy and Side Effects: Summary. 2003 Mar. In: *AHRQ Evidence Report Summaries*. Rockville (MD): Agency for Healthcare Research and Quality (US); 1998-2005. 76. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK11897/>
- [44] Ashtary-Larky D, Ghanavati M, Lamuchi-Deli N, et al. Rapid Weight Loss vs. Slow Weight Loss: Which is More Effective on Body Composition and Metabolic Risk Factors?. *Int J Endocrinol Metab*. 2017;15(3):e13249. Published 2017 May 17. doi:10.5812/ijem.13249
- [45] Williams MH. Dietary supplements and sports performance: introduction and vitamins. *J Int Soc Sports Nutr*. 2004;1(2):1-6. Published 2004 Dec 31. doi:10.1186/1550-2783-1-2-1
- [46] Giannopoulou I, Noutsos K, Apostolidis N, Bayios I, Nassis GP. Performance level affects the dietary supplement intake of both individual and team sports athletes. *J Sports Sci Med*. 2013;12(1):190-6. Published 2013 Mar 1.
- [47] Ernst E. Toxic heavy metals and undeclared drugs in Asian herbal medicines. *Trends Pharmacol Sci*. 2002 Mar;23(3):136-9. Review. PubMed PMID: 11879681.
- [48] McCabe SE, Brower KJ, West BT, Nelson TF, Wechsler H. Trends in non-medical use of anabolic steroids by U.S. college students: results from four national surveys. *Drug Alcohol Depend*. 2007; 90(2-3):243-51.
- [49] Ganesan K, Pellegrini MV. Anabolic Steroids. [Updated 2018 Nov 13]. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK482418/>
- [50] Maughan RJ, Shirreffs SM. Nutrition for sports performance: issues and opportunities. *Proc Nutr Soc*. 2012 Feb;71(1):112-9. doi: 10.1017/S0029665111003211. Epub 2011 Oct 17. PubMed PMID: 22000743.

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