Annals of R.S.C.B., ISSN:1583-6258, Vol. 23, Issue 2, 2019, Pages. 262 - 268
Received 15 October 2019; Accepted 22 December 2019.

Effect of Doping and Purifying Agents Used by Male Bodybuilders on Parathyroid Activity, Ca^{+2} and Sexual Hormones

Nael Mohammed Sarheed
Medicine College / AL-Muthanna Uni.
Email: Nael.serheed@mu.edu.iq

Abstract

It has previously been found in some studies that the use of anabolic hormones and steroids has an adverse effect on the sexual status of bodybuilding athletes, and the use of purifying substances to remove these effects and compensate for the decrease in the effectiveness of some glands also had an impact on many parts of the body due to unhealthy use among athletes. Therefore, this study aimed to investigate the changes occurring in the effectiveness of the parathyroid gland through its hormonal secretion and the extent of its impact on the level of blood calcium, as well as the sexual hormonal status of bodybuilding athletes in the last period of the hormonal cycle. 16 samples were taken from the bodybuilding athletes' blood and were divided into two groups. The first group represented athletes at the end of the hormonal cycle, and the second group represented athletes without taking hormonal substances. Then, the levels of parathyroid hormone and calcium were measured, in addition to the sex hormones (testosterone and estradiol). The results of the current study found a significant increase in the level of parathyroid hormone, which accompanied the increase in blood calcium. As for the sex hormones, they were opposite, as an increase in the male hormone (testosterone) was observed, and a significant decrease in the female hormone (estradiol). We concluded that the hormonal cycle plays an important role in replacing calcium in athletes as a result of high parathyroid hormone. As well as maintaining levels of sex hormones within normal limits.

Keywords: Anabolic steroids, bodybuilders, Sex hormones, PTH, Calcium

Introduction

The materials used for building and develop muscle tissue in bodybuilding athletes are very important during the athlete hormonal cycle, as the athlete is initially given building materials to increase testosterone through nutritional supplements , some of which are anabolic steroids such as Testosterone suspension, Sustanon, and others [(1)]. Then the bodybuilder is prepared with detergents (purifying) that are considered aromatase inhibitors, such as Clomid, Nolvadex, T3, and others [(2)], which are used to treat breast cancer in women [(3)], and play a role in reactivating testosterone-secreting cells in the testicle of the athletes, in addition to preventing the conversion of hormonal substances into estrogen to avoid gynecomastia, and the emergence of other feminine characteristics among bodybuilders [(1)].

Studies have shown that these substances have significant pathological effects on public health, as they were found to play a major role in testicular atrophy and pancreatitis [(4)], as well as dysfunction in the liver, thyroid and kidney failure resulting from high concentrations of these substances [(5)(6)(7)]. Therefore, this study came to demonstrate the side effects of these

Annals of R.S.C.B., ISSN:1583-6258, Vol. 23, Issue 2, 2019, Pages. 262 - 268
Received 15 October 2019; Accepted 22 December 2019.

doping and purifying substances on the level of thyroid hormone and calcium associated with androgen hormones during the hormonal cycle of bodybuilders.

Materials and Methods

Experiment Design

16 Blood samples were collected from bodybuilding athletes in the sports halls with weight (90-115kg) and age (25-35 year), some of these athletes were taking various substances for the purpose of building muscles in their bodies during the so-called hormonal cycle, which extends for 60-90 days and includes taking hormonal substances that help increase testosterone, such as Sustanon (500 mg) and boldenone (400 mg) daily. During this period, after three days of taking anabolic steroids, other purifying substances called detergents are taken, which include Arimidex (Anastrazole) by 2.5 mg daily, and Nolvadex (Tamoxifin) for 5 mg daily) throughout the cycle. Some of the concentrations of these substances are controlled according to measuring the percentage of testosterone monthly in laboratories and assessing the body condition of bodybuilding athletes.

The athletes include 16 sample classify to two group , First group include 8 sample for athletes with hormonal cycle, and the second group include 6 athletes without hormonal cycle. After taking the samples, they were stored in special tubes, after which the serum was isolated by centrifugation, and the samples were kept in the refrigerator until the required tests were performed.

The parathyroid hormone test was performed according to method [8], while the calcium concentration in the serum was measured according to [9]. As for testosterone and estradiol was measured according to[10].

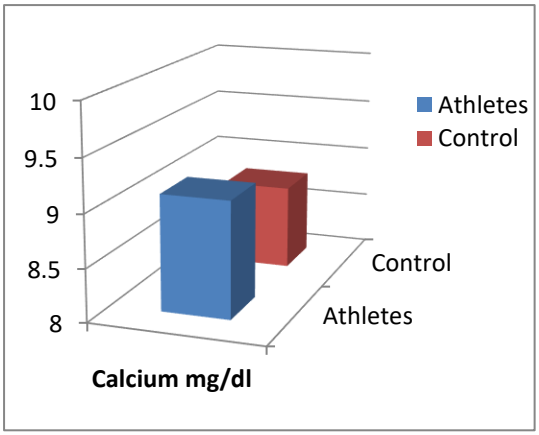
Statistical analysis

Statistical comparisons were made according to the SPSS program, and pairwise comparison was used using the T-test for all the resulting data according to [11] method**.**

Results & Dissection

Studies have indicated that there is a significant impact of the various supplements and materials used when building muscle size in athletes on various parts of the body, including the heart, muscles, pancreas, thyroid gland, reproductive organs, psychological state, and others (1-1). This topic aimed to follow up on changes in the effectiveness of the parathyroid gland and sex hormones in bodybuilding athletes in the late stages of the hormonal cycle. This study showed, through the results of tests on the athletes' blood, that there was a significant increase ($P < 0.05$) in the percentage of parathyroid hormone and the calcium level of athletes who take doping and purifying substances after completing a period for more than two months of the hormonal cycle when compared to the group of non-using athletes who represented Control

Annals of R.S.C.B., ISSN:1583-6258, Vol. 23, Issue 2, 2019, Pages. 262 - 268
Received 15 October 2019; Accepted 22 December 2019.



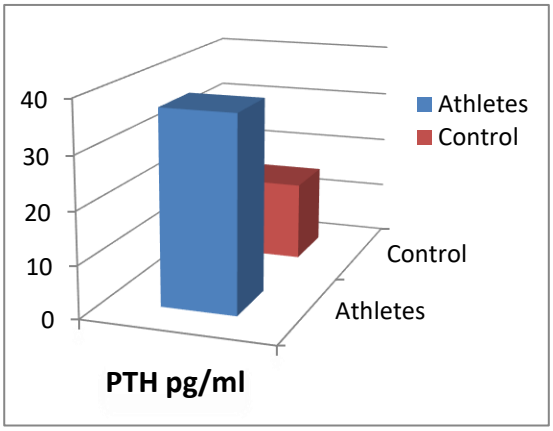


Figure 1: Calcium levels for Athletes with a hormonal cycle and a control groups
Figure 2: Parathyroid hormone levels for Athleteswith a hormonal cycle and a control groups

This confirms our results among the vital indicators that include an increase in the percentage of calcium combined with an increase in the parathyroid hormone, which works to convert vitamin D to the active form in the kidneys, which helps withdraw calcium from the intestines, kidneys, and bones into the blood, which causes an increase in the level of this element in the serum [(12)(33)]. Therefore, the study agreed with what some researchers stated, indicating that the use of estrogen inhibitors, including Arimidex, works to inhibit the density of bone elements due to the release of this element from bone tissue as a result of the effect of the iPTH hormone (which is the active form of parathyroid hormone), for works indirectly on Osteoclasts that transformed into their active form, which increases the process of bone resorption and leads to an increase in the level of calcium in the blood in a study on breast cancer patients [(13)(31)]. These results also support what was stated by [(2)(14)] that taking Arimidex leads to an increase in PTH and Calcium in an experiment on elderly women that included 65 healthy and sick cases. . Also, the increase in calcium in this study may come from hyperparathyroidism, according to what was described by [(15)], and what was confirmed by [(16)] of an increase in the level of calcium accompanied by an increase in parathyroid hormone after taking tamoxifen (Nolvadex) in patients with breast cancer. In addition to what was mentioned [(17)] about the effect of the drug Anastrazole (Arimidex) in increasing the concentration of calcium in the blood, which may be due to the interaction of aromatase inhibitors with calcium receptors on the epithelial tubules in the nephron, which inhibits the excretion of calcium into the urinary filtrate [(18)]. In addition to other studies observed in breast cancer patients related to the binding of these substances to hormonal receptors, including parathyroid hormone, which increases the probability of hyperparathyroidism [(19)(20)(21)].

As for the level of sexual hormones among athletes who used doping and purifing substances, it appeared opposite, as testosterone was found to be significantly high ($P < 0.05$) and by a large percentage among athletes when compared to the levels of this hormone in the control group, which represents athletes who did not toke any substance (Figure 3).

Annals of R.S.C.B., ISSN:1583-6258, Vol. 23, Issue 2, 2019, Pages. 262 - 268
Received 15 October 2019; Accepted 22 December 2019.

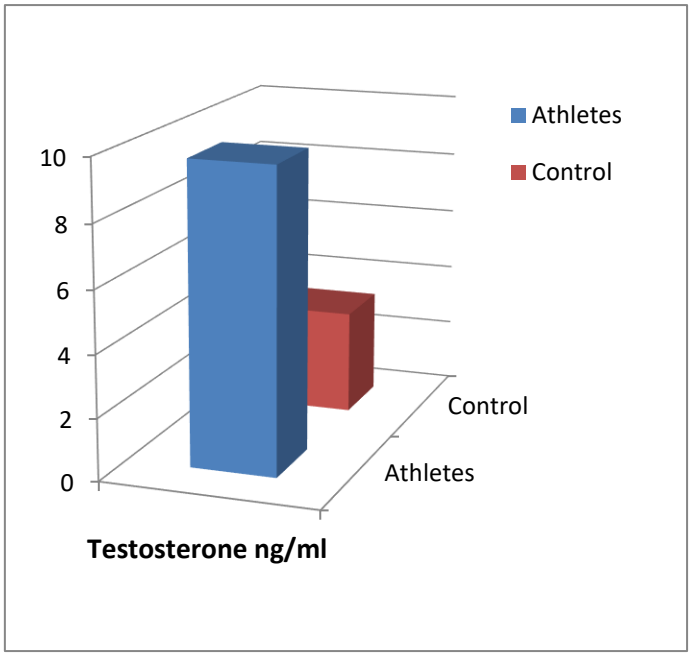


Figure 3: Testosterone levels for Athletes with a hormonal cycle and a control groups

While, on the contrary, the level of estradiol in athletes after using the substances appeared very low and significantly ($P < 0.05$) when comparing its levels to the blood of athletes who did not participate in the hormonal cycle and who represented the control group (Figure 4).

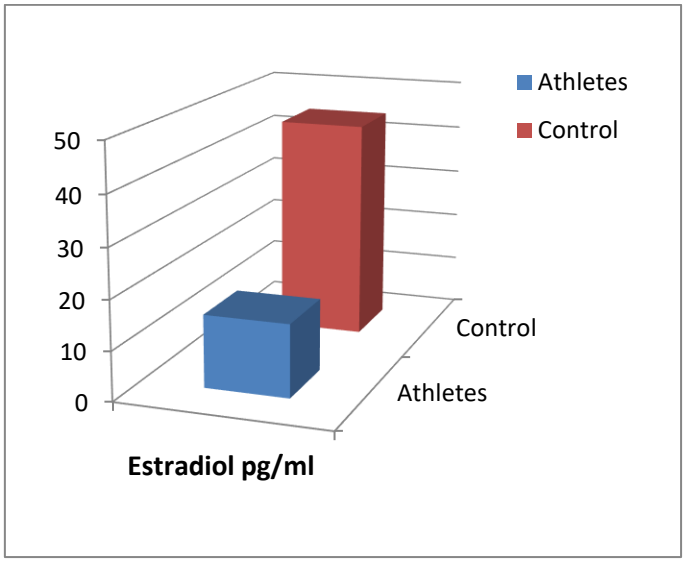


Figure 4: Estradiol levels for Athletes with hormonal cycle and a control groups

Previous studies reported that the use of hormonal supplements, which are considered one of the androgenic substances, helps to increase testosterone at the beginning of the cycle, but the condition reverses at the end of the hormonal cycle, causing a decrease in the level of this hormone and leading to side effects, including infertility and the appearance of gynecomastia in athletic men [(22)], Other researchers pointed out that anabolic steroids, which are considered aromatase inhibitors and mediators of estrogen receptors, are completely unknown in terms of their effect on bodybuilding athletes because studies on these cases are usually accompanied by doping substances such as Sustanon, which works to reverse the effect

[23]. Here, studies show that the effect of anabolic substances works to increase the level of testosterone at the beginning of the hormonal cycle in athletes, but this level gradually decreases due to its conversion to estradiol after hormonal cycle, which adds non-existent feminine characteristics for the man, while purifying substances (such as Tamoxifen and Nolvadox) that are necessary within the hormonal cycle works to inhibit this transformation, which increases the level of testosterone and reduces estradiol [24][25][26]. This explains the high level of testosterone and low level of estradiol in athletes at the end of the hormonal cycle in our study. On the other hand, [14] indicated that the use of tamoxifen in patients with breast cancer led to a decrease in the level of estradiol in women, and that the presence of estrogen receptors leads to the conversion of estrone into estradiol by the aromatase enzyme, which works to convert testosterone and androstenedione into estrogen compounds, including estradiol and estrone respectively in a process called aromatization in some tissue in the body as ovaries, liver, brain, muscle and breast [27][28]. While the presence of anti-estrogens and progestational agents leads to weakening this transformation by inhibiting this enzyme to the lowest possible level, this is done by inhibiting the estrogen biosynthesis pathway at the final step, creating an aromatic ring in the steroid molecule that prevents the conversion of androgens to estrogens [29] . which reflects the effect of Nolvadex and Arimidex in inhibiting the level of estradiol, noting the greater effectiveness of Arimidex in this subject [31][6], and the competitive binding of aromatase to heme of the cytochrome P450 group leads to a weakening of the biosynthesis of estrogen, and this reflects the mechanism of inhibition of the aromatase enzyme [33]. is what can be pointed out in our study in the decrease in the level of estradiol as a result of the use of Tamoxifen and Arimidex, which are considered inhibitors of the aromatase enzyme. According to what was mentioned, there is a widespread use of aromatase inhibitors as a treatment for breast cancer in women, resulting in metabolic disturbances in most cases. Therefore, these potential changes must be monitored with the use of these compounds for long-term periods[29].

Conclusions

We concluded from our study that purified substances had a clear role in activating the activity of the parathyroid gland and its importance for the level of calcium in the blood in athletes, as well as another important role in maintaining the normal level of some hormonal blood parameters such as testosterone and estradiol in male body building athletes and concealment possible feminine characteristics due to the hormonal substances used.

References

1- Lee, T. W., Kyungo, E. B., Ha Nee, H. , Park, J. H. , Jeon, D., Cho, H. S. and Chang, s. h. .Severe hypokalemic paralysis and rhabdomyolysis occurring after binge eating in a young bodybuilder: Case report. Medicine (Baltimore) 2017 Oct; 96(40): e8251. Published online 2017 Oct 27. doi: 10.1097/MD.0000000000008251

2- Houghton, J. Comprehensive side-effect profile of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: long-term safety analysis of the ATAC trial, The lancet oncology. Volume 7, Issue 8, August 2006, Pages 633-643.DOI:https://doi.org/10.1016/S1470-2045(06)70767-7

3- Buzdar A, Jonat W, Howell A, Yin H and Lee D on behalf of the Arimidex International Study Group (1997) Significant improved survival with Arimidex (anastrozole) versus

megestrol acetate in postmenopausal advanced breast cancer: updated results of two randomized trials (abstract 545). *Proc Am Soc Clin Oncol* 16: 156a

4- Ngo, D., Bautista, J. , Green, C. S. , Gulati, A. & Chandana Lall.Cancer therapy related complications in the liver, pancreas, and biliary system: an imaging perspective. Insights Imaging (2015) 6:665–677. DOI 10.1007/s13244-015-0436-7.

5- Menna M Abdel-Dayem and Mohamed S Elgendy, Effects of chronic estradiol treatment on the thyroid gland structure and function of ovariectomized rats, *BMC Research Notes* 2009, 2:173 doi:10.1186/1756-0500-2-173

6- M Dowsett, JS Tobias, A Howell3, GM Blackman, H Welch1, N King, R Ponzone, M von Euler and M Baum, The effect of anastrozole on the pharmacokinetics of tamoxifen in post-menopausal women with early breast cancer. British Journal of Cancer (1999) 79(2), 311–315

7- Merino García E, Borrego Utiel FJ, Martínez Arcos MÁ, Borrego Hinojosa J, Pérez del Barrio MP. Consecuencias renales del uso de esteroides anabolizantes y práctica de culturismo. Nefrología. 2018;38:101–103.

8- Brandi ML, Bilezikian JP, Shoback D, et al. Management of hypoparathyroidism: summary statement and guidelines. J Clin Endocrinol Metab. 2016;101(6):2273-83.

9- Clinical Biochemistry Laboratory Formulary Working Group, Parathyroid Hormone and calcium status testing, Laboratory Medicine Program Eastern Health Rm. 1J442, Health Sciences Centre, 300 Prince Philip Drive, St. John's, NL A1B 3V6.

10- Clinical Chemistry Branch, Division of Laboratory Sciences , National Center for Environmental Health, Laboratory Procedure Manual, CDC , Total Estradiol and Total Testosterone NHANES 2015-16 Method No: 1033.

11- S. A. Al-Ukaelii, and S. M. Al- Shaeb, Statically Analysis by used SPSS Program. Al-Shoroq house for Publishers and advertisement Amaan, Jordan, 1998.

12- Borissova AM, Tankova T, Kirilov G *et al.* (2003): The effect of vitamin D3 on insulin secretion and peripheral insulin sensitivity in type 2 diabetic patients. Int J Clin Pract., 57: 258-61.

13- Gosink, J. Parathyroid hormone, calcitonin and vitamin D testing in calcium and bone metabolic disorders, EUROIMMUN AG, Luebeck, Germany, MEDLAB MAGAZINE ISSUE 2 2015, 026-028.

14- PRODUCT MONOGRAPH, PrDom-ANASTROZOLE,Book, 1 mg Non-Steroidal Aromatase Inhibitor, DOMINION PHARMACAL, December 1, 2016, Submission Control No.: 185300.

15- Fraser WD. Hyperparathyroidism. Lancet. 2009 Jul 11;374(9684):145-58. doi: 10.1016/S0140-6736(09)60507-9.

16- Punda, M. et al. (2020). PRIMARY HYPERPARATHYROIDISM AND SERUM CALCIUM IN BREAST CANCER PATIENTS EVALUATED FOR LOW BONE MASS A SINGLE CENTER EXPERIENCE, Acta Clin Croat, Vol. 60, No. 4,, Acta Clin Croat; 60:617-626, doi: 10.20471/acc.2020.60.04.08.

17- Di Nardo G, Gilardi G. Human aromatase: perspectives in biochemistry and biotechnology. Biotechnol Appl Biochem. 2013; 60(1):92-101.

18- Brown EM, Gamba G, Riccardi D, Lombardi M, Butters R, Kifor O, *et al.* Cloning and characterization of an extracellular Ca(2+)-sensing receptor from bovine parathyroid. Nature. 1993;366(6455):575-80. doi: 10.1038/366575a0.

19- Järhult J. Anastrozole can cause severe hypercalcaemia mimicking primary hyperparathyroidism. Breast Cancer [Internet]. 2014 May;21(3):379-81.

20- Ipekci SH, Baldane S, Ozturk E, Araz M, Korkmaz H, Colkesen F, *et al.* Letrozole induced hypercalcemia in a patient with breast cancer. Case Rep Oncol Med [Internet]. 2014;2014: 608585.

21- Camacho PM, Dayal AS, Diaz JL, Nabhan FA, Agarwal M, Norton JG, *et al*. Prevalence of secondary causes of bone loss among breast cancer patients with osteopenia and osteoporosis. J Clin Oncol [Internet]. 2008 Nov 20;26(33):5380-5.

22- Kheloufi F, Default A, Blin O, Micallef J. Investigating patient narratives posted on Internet and their informativeness level for pharmacovigilance purpose: The example of comments about statins. Therapie 2017;72:483–90.

23- Saugy M, Robinson N, Saudan C, Baume N, Avois L, Mangin P. Human growth hormone doping in sport. Br J Sports Med . 2006 ; 40 : i35. doi: 10.1136/bjsm.2006.027573.

24- Boccardo F, Rubagotti A, Battaglia M, Di Tonno P, Selvaggi FP, Conti G, et al. Evaluation of tamoxifen and anastrozole in the prevention of gynecomastia and breast pain induced by bicalutamide monotherapy of prostate cancer. J Clin Oncol 2005;23:808–15.

25- Kunath F, Keck B, Antes G, Wullich B, Meerpohl JJ. Tamoxifen for the management of breast events induced by non-steroidal antiandrogens in patients with prostate cancer: a systematic review.BMC Med 2012;10:96.

26- Schlegel PN. Aromatase inhibitors for male infertility. Fertil Steril 2012;98:1359–62.

27- Berstein L, Maximov S, Gersgfeld E, Meshkova I et al. (2002) Neoadjuvant therapy of endometrial cancer with the aromatase inhibitor letrozole: endocrine and clinical effects. *Eur J Obstet Gynecol Reprod Biol* 105: 161–165.

28- Simpson ER, Dowsett M (2002) Aromatase and its inhibitors: significance for breast cancer therapy. *Recent Prog Horm Res* 57: 317–338

29- Michael J. Parnham , J. Bruinvels and Milestones in Drug Therapy (MDT), Aromatase inhibitors(2006). ISBN 3-7643-7199-4 Birkhäuser Verlag, Basel - Boston – Berlin.

30- Sarheed, N. M., kokaz , O. F and Muhammed Ridh, D. A. The Toxicity of Castor Beans and its Treatment with Doxycycline in Local Rabbits. International Journal of Pharmaceutical Quality Assurance 2018; 9(2); 208-216.

31- Geisler J, King N, Dowsett M, Ottestad L, Lundgren S, Walton P, Kormeset PO and Lønning PE (1996) Influence of anastrozole (Arimidex), a selective, nonsteroidal aromatase inhibitor, on in vivo aromatization and plasma oestrogen levels in post-menopausal women with breast cancer. *Br J Cancer* 74:1286–1291

32- Sarheed, N. M., Fajer, A. N. and Hussein, M. N.(2018), STUDY OF THE PATHOLOGICAL EFFECTS TO ONE OF FOOD ADDITIVES IN MALE RATS (GELATIN 441). *Biochem. Cell. Arch.* Vol. 18, No. 1, pp. 225-233.

33- Sanford M, Plosker GL. Anastrozole: a review of its use in postmenopausal women with early-stage breast cancer. Drugs. 2008; 68(9):1319-40.