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Short Communication

Combined usage of testosterone and nandrolone may cause heart damage

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The aim of this study is to determine the effects of combined application of testosterone and nandrolone on male rabbits during adolescence period for biochemical values which are indicators of damage to heart, liver and kidney. Seven male New Zealand white rabbits, 60-days old, were used in this study. Testosterone (10 mg/kg) + nandrolone deconoate (10 mg/kg) were injected simultaneously to the rabbits in an intramuscular manner once in 1 week for a period of 12 weeks. Blood samples were taken in 0, 4, 8 and 12 weeks. Serum creatine kinase-MB, lactate dehydrogenase, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl-transferase, creatinine and blood urea nitrogen were measured with an auto-analyzer. Combined use of testosterone and nandrolone caused ($p < 0.05$) increase in serum creatine kinase-MB activity, but no statistical changes ($p > 0.05$) were determined in other parameters. As a result, it can be concluded that the use of testosterone plus nandrolone simultaneously during early ages may cause heart damage.

Key words: Testosterone, nandrolone, creatine kinase-MB.

INTRODUCTION

The term testosterone has first been used as sexuality hormone during the 1930s as the combination of 'testo↔testes', 'ster↔sterol' and 'one↔ketone' (Handelsman, 2006; Dotson, 2007). Testosterone is produced in leydig cells (Hartgens, 2004) and it is effective in spermatogenesis, development of secondary sexual characters, release of gonadotropine and stimulation of protein synthesis in an anabolic manner (Wu, 1997; Basaria et al., 2001; Hartgens, 2004). Nandrolone (19-nortetosterone, 17β-hydroxyestr-4en3-one) has been synthesized during the 1950s for the first time. It displays a high affinity to androgen receptors and it has both anabolic and androgenic qualities (Ayotte, 2006; Lumia et al., 2010).

Testosterone and nandrolone are used in the evaluation of the clinical potential of male fertility, kidney failure, aplastic anemia, delayed adolescence, asthenia based on Acquired immune deficiency syndrome (AIDS), protection of immune system after cancer, treatment of hemodialysis patients, osteoporosis, cachexia, trauma or the post-surgery recovery period (Ayotte, 2006; Kerr, 2007).

It is seen that the use of anabolic androgenic steroids (AAS), particularly by young men, have dramatically increased in recent years. It has been used to increase the mass and weight of the body and power to compete, to better their appearances and to improve self-esteem. One of the most common misuses of ASS is testosterone which is an endogen androgen. Testosterone does not only have an endogen effect but it also has an excellent anabolic effect (Lumia et al., 2010). The study that has been conducted has shown that 1 to 2% of young girls and 4 to 6 % of young boys have taken steroids, even if it is just once in a lifetime (Marshall et al., 2009). Misuse by sportsmen cause ethical problems as well (Bhasin et al.,

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Abbreviations: AIDS, Acquired immune deficiency syndrome; **AAS,** anabolic androgenic steroids; **WADA,** world anti doping agency; **CK-MB,** creatine kinase-MB; **LDH,** lactate dehydrogenase; **ALP,** alkaline phosphates; **ALT,** alkaline aminotransferase; **AST,** aspartate aminotransferase; **GGT,** gamma glutamyl transferase; **BUN,** urea.

1996). World Anti Doping Agency (WADA) has stated that sportsmen use testosterone, nandrolone and stanazolol (Handelsman 2006).

AAS may cause bile flow disorders, sensitivity against insulin, disorders in lipid metabolism, hyper-tension, testicular atrophy, gynecomastia, liquid retention, tendon injuries, nose bleeds, hepatic and renal dysfunction, sleep disorders, frequent cold, tachycardia, cardio-megaly, muscle pain, increase in atherosclerosis, acne, increase in sebum production in men, hirsutizm, virilization in women and sudden death (Bhasin et al., 1996; Basaria et al., 2001; Modlinski et al., 2006; Casavant, 2007; Marshall, 2009).

Values of serum biochemistry provide us information about organ and system damages in a creature. Creatine kinase-MB (CK-MB) (Dickerman et al., 1999) increases in heart damage, whereas lactate dehydrogenase (LDH) increases in myocardium, liver and musculoskeletal diseases (Turgut, 2000). Liver damage indicators are alkaline phosphates (ALP), alkaline aminotransferase (ALT), aspartate aminotransferase (AST) and gamma glutamyl transferase (GGT), whereas urea (BUN) and creatinine are kidney damage indicators (Bartley, 1989; Finco, 1989; Kramer, 1989). No information regarding the effects of long term combined use of testosterone and nandrolone during youth on serum biochemical values have been obtained in the researches that have been made.

The aim of this study is to examine effects of applying testosterone and nandrolone on male rabbits in adole-scence on the damage indicators regarding heart, liver and kidney.

MATERIALS AND METHODS

Seven New Zealand white rabbit of 60 days old (1000 to 13000 g, SÜDAM, Konya, Turkey) were used in the study. Animals were fed *ad libitum* during the experiment. The research has been confirmed by the Veterinary Faculty Ethic committee. Once in a week, 10 mg/kg testosterone (Sustanon® 250 amp, Organon ilaçları A.S, Istanbul, Turkey) + 10 mg/kg nandrolone deaconate (DECA 1000 flk. Gen-shi labs.co. Osaka, Japan) was injected into the animals in an intramuscular manner. Blood was taken from auricular artery in weeks 0, 4, 8 and 12. Levels of CK-MB, LDH, ALP, ALT, AST, GGT, creatinine and BUN were determined in auto-analyzer (IL-300 Instrumentation laboratory Milano, Italy) from the serums that have been obtained.

Statistical analysis

Results of the study were evaluated by analysis of variance (ANOVA) and Tukey test (SPSS 10.0). $P < 0.05$ value has been accepted as significant in statistical terms.

RESULTS AND DISCUSSION

Effect of testosterone + nandrolone application on adolescent male rabbits on serum biochemical values is given in Table 1. Testosterone and nandrolone application causes increase in CK-MB level ($P < 0.05$). Changes in LDH, ALP, ALT, AST, GGT, CREAT and BUN levels have been determined to be within the reference range.

Testosterone and its derivatives, which have been used for treatment since 1940s, are being misused by some sportsmen (Kerr et al., 2007; Handelsman, 2006). Testosterone and nandrolone application on adolescent rabbits in this study caused an increase ($P < 0.05$) in serum CK-MB level (Table 1).

Similarly, while an increase is observed in CK-MB with the male rats to which testosterone has been applied (Lok et al., 2010), no increase has been observed in CK-MB levels with female rats (Tasgin et al., 2010). Serum CK-MB levels are being used in the diagnosis of cardiovascular system disorders (Brancaccio et al., 2006). It has not been observed in literature reviews that combined use of testosterone and nandrolone has effects on serum CK-MB levels. Combined use of testosterone and nandrolone may cause heart damage especially for adolescent males.

LDH levels in the current study have been determined to be above ($P < 0.05$) the reference range during first sampling time (Table 1). In this study, in which enzyme levels from childhood to advanced ages have been studied, it is observed that LDH levels have decreased for young and adolescent people (Lockitch et al., 1988). It may be said also that the reason why LDH levels are high at the beginning is because of the early ages. Also, the high ($P < 0.05$) levels determined for GGT in the day 0 may result from the fact that it has been high during early ages, as it is the situation in LDH.

Serum ALP, ALT, AST and GGT levels increases in liver damage (Turgut, 2000; Er and Yazar, 2010). Although it has been stated that these values increased in the studies which reported the effect of AAS on liver damage (Hartgens et al., 2004; Vieira et al., 2008; Lok et al., 2010; Tasgin et al., 2010), these values have been determined to be within reference range in the current study (Altunok et al., 2002; Hernandez-Divers, 2004; Yazar et al., 2004) (Table 1). The result of this study may be as a result of the applied medicine, dose and animal breed differences.

Although there have been some changes in creatinine and BUN levels in the current study (Table 1), these differences have been determined to be within reference range (Elmas et al., 2006; Elmas et al., 2008).

Conclusion

As a conclusion, it can be said that long term testosterone and nandrolone use in early ages may cause heart damage in young ages. However, this study should be supported especially with histopathological researches.

Table 1. Effects of testosterone + nandrolone on serum organ damage markers (mean±SE).

Weeks	0	4	8	12	Reference range
CK-MB (U/L)	3114±327^{b}	1895±343^{b}	2695±592^{b}	4737±166^{a}	-------
LDH (U/L)	1188±122^{a}	355±30.3^{c}	226±17.6^{c}	754±101^{b}	34-500
ALP (U/L)	183±15.7^{a}	156±14.2^{ab}	109±12.0^{bc}	60.8±7.33^{c}	16-231
ALT (U/L)	51.8±3.37^{a}	58.0±6.55^{a}	81.2±15.4^{a}	52.3±5.13^{a}	22-87
AST (U/L)	59.6±7.53^{a}	30.1±5.32^{b}	29.2±6.16^{b}	58.2±7.54^{a}	14-113
GGT (U/L)	16.2±1.72^{a}	12.3±2.22^{ab}	9.62±0.77^{b}	8.87±0.93^{b}	0-7
Creatinine (mg/dL)	0.64±0.06^{c}	0.77±0.05^{bc}	0.88±0.04^{ab}	1.04±0.06^{a}	0.6-1.97
BUN (mg/dL)	32.7±1.88^{b}	40.6±4.40^{ab}	40.8±1.39^{ab}	46.2±3.49^{a}	17-48

Different letters on the same line are statistically significant (Tukey test, $P < 0.05$).

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