Anabolic Steroid and nutritional supplements effect on kidney

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Abstract: Background: Frequent use of anabolic steroids and dietary supplements for the purpose of the muscle mass is common among body builders. Recent evidence indicates that anabolic steroids are directly toxic to glomeruli and that segmental sclerosis is the result of podocyte loss mediated by apoptosis through a podocyte androgen receptor. The high-protein intake has been of concern to nephrologists because it increases glomerular filtration rates and is experimentally associated with glomerular hyperfiltration and FSGS. The aim of the present study was to assess and compare the effect of anabolic steroids and other nutritional supplements on kidney outcomes.

Methods: Twenty male body builders volunteered to participate in this study, age between (20 and 35 years). Volunteers were divided into two groups. Group 1 (Steroid group) consisted of ten male volunteers use anabolic steroids (more than two years and less than 5 years) with concomitant use of whey protein, creatine monohydrate and Branched chain amino acids intermittently for more than 2 years. Group 2 (Non-Steroid group), included ten male volunteers use whey protein, creatine monohydrate and Branched chain amino acids intermittently for more than two years.

Results: There is significant increase in the amount of protein in 24 hours of collected urine (mg/24 hrs.) in steroid group (group 1) when we compare its level to non steroid group (group 2) (24 hrs. urine ptn: 859.50 ± 805.72 vs. 128.50 ± 48.25, p<0.001).

Conclusion: Long use of AASs could produce renal effects as variable elevations in serum creatinine and development of substantial proteinuria.

Keywords: anabolic steroids, nutritional supplements, FSGS

1. Introduction
1.1. Background

Frequent use anabolic steroids and dietary supplements to increase muscle mass is common among body builders (Fink et al., 2009). Main nutritional supplements are protein, creatine and Branched-chain amino acids (Martin et al., 2005). Herlitz et al., (2010) reported 10 body builders who developed renal insufficiency and focal segmental glomerulosclerosis (FSGS) while taking anabolic steroids and protein and creatine supplements with a daily protein intake of 300–550 g/day. The high-protein intake has been of concern to nephrologists because it increases glomerular filtration rates and is experimentally associated with glomerular hyperfiltration and FSGS (Martin et al., 2005). Recent evidence indicates that anabolic steroids are directly toxic to glomeruli and that segmental sclerosis is the result of podocyte loss mediated by apoptosis through a podocyte androgen receptor (Pendergraft et al., 2014). Creatine powder is a muscle building supplement. Creatine is used by a large number of athletes (Cooper et al., 2012). The number of reported adverse events is small and usually associated with exercise-induced acute renal failure and rhabdomyolysis during intense training but even with moderate exercise (Sandhu et al., 2002). We aim to investigate the extent of kidney affection after prolonged use of anabolic steroids and other nutritional supplements.

1.2. Research objective

The aim of the present study is to assess and compare the effect of anabolic steroids and other nutritional supplements on kidney outcomes.

2. Materials and methods
2.1. Ethics

A written informed consent was obtained from all candidates. The study complies with the Declaration of Helsinki. Twenty male body builders volunteered to participate in this study, age between (20 and 35 years), with no history of medical disease (Diabetes mellitus, Hypertension, heart disease or previous kidney disease).

2.2. Data collection

Between August 2014 and December 2015; 50 volunteers were screened and 20 were considered eligible for the trial. After 30 exclusions. All volunteers in the study are training regularly for the past 5 years. Volunteers were divided into 2 groups:

1) Group 1 (Steroid group): Ten male volunteers use anabolic steroids (more than 2 years and less than 5 years) with concomitant use of whey protein, creatine monohydrate and Branched chain amino acids intermittently for more than 2 years.
2) Group 2 (Non-Steroid group): Ten male volunteers use whey protein, creatine monohydrate and Branched chain amino acids intermittently for more than 2 years.

All volunteers assigned to the study were subjected to complete history and physical examination; AND Laboratory investigations including complete blood count, erythrocyte sedimentation rate, serum urea, serum creatinine, creatinine clearance, urine analysis and 24 hour protein excretion.

2.3. Statistical analysis

Comparison between normally distributed parameters in the three studied groups was performed using one way AVOVA followed by Least significant difference test if significant results was recorded. Comparison between not normally distributed parameters in the three studied groups was performed using Kruskal Wallis ANOVA test followed by Mann Whitney test if significant results was recorded. Comparison between parameters in the two studied groups was performed using either unpaired t test or Mann Whitney test whenever it was appropriate. Comparison between categorical data was performed using Chi square test. Correlation between different parameters was performed using Spearman rank correlation coefficient. Receiver-operating characteristic (ROC) curve was used to calculate the diagnostic indices of Th17, T reg and Th17/T reg ratio. The data were considered significant if p value was ≤ 0.05 and highly significant if p value < 0.01.

Statistical analysis was performed with the aid of the SPSS computer program (version 12 windows).

3. Results

Results were expressed as means ± standard deviation of the means (SD) or number (%). Between August 2014 and December 2015; 50 volunteers were screened and 20 were considered eligible for the trial. After 30 exclusions, all volunteers in the study are training regularly for the past 5 years. A written informed consent was obtained from all candidates. The study complies with the Declaration of Helsinki. According to our findings, there is non-significant increase in S. Cr. in both: steroid group (group 1) (S. Cr: 1.76 ± 0.25) and the non-steroid group (group 2) (S Cr: 1.57 ± 0.12). Also, there is non-significant increase in S. Cr. in steroid group (group 1) when we compare its level to non-steroid group (group 2) (S Cr: 1.76 ± 0.25 vs. 1.57 ± 0.12). Our findings showed that there is non-significant increase in the amount of protein in 24 hours of collected urine (mg/24 hrs.) in both: steroid group (group 1) (24 hrs. urine ptn.: 859.50 ± 805.72) and the non-significant increase in protein in 24 hours of collected urine in the non-steroid group (group 2) (24 hrs. urine protein: 128.50 ± 48.25). Finally, the study showed that there is significant increase in the amount of protein in 24 hours of collected urine (mg/24 hrs.) in steroid group (group 1) when we compare its level to non-steroid group (group 2) (24 hrs. urine ptn.: 859.50 ± 805.72 vs. 128.50 ± 48.25, p<0.001).

Table 1: represents comparison between the 2 groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1: steroid (n= 10)</th>
<th>Group 2: Non steroid (n= 10)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs.)</td>
<td>29.00 ± 4.06</td>
<td>28.50 ± 3.63</td>
<td>0.704</td>
</tr>
<tr>
<td>BMI</td>
<td>34.50 ± 2.99</td>
<td>33.70 ± 4.16</td>
<td>0.732</td>
</tr>
<tr>
<td>Hormone use duration (yrs.)</td>
<td>4.20 ± 0.79</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Supplements diet duration</td>
<td>4.80 ± 0.42</td>
<td>4.50 ± 0.97</td>
<td>0.282</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>1.76 ± 0.25</td>
<td>1.57 ± 0.12</td>
<td>0.054</td>
</tr>
<tr>
<td>Ptn. 24 hrs. urine (mg/24 hrs.)</td>
<td>859.50 ± 805.72</td>
<td>128.50 ± 48.25</td>
<td>0.003**</td>
</tr>
</tbody>
</table>

Data were expressed as mean ± SD; p> 0.05= not significant; **; p< 0.01= highly significant.

4. Discussion

Frequent use of anabolic androgenic steroids (AASs) and dietary supplements such as protein, creatine and branched chain amino acids by athletes to improve performance in certain sports, such as bodybuilding and powerlifting and to increase muscle mass is common (Almukhtar et al., 2015). It is well known that AASs are family of hormones which include testosterone as well as its naturally occurring and synthetic derivatives, which have been used to increase muscle mass and decrease body fat since the 1950s (Pendergraft et al., 2014). However, several studies suggest that approximately 30% of AASs users develop dependence and would therefore be at a higher risk for developing the medical consequences of protracted abuse (Kanayama et al., 2009). It is noteworthy to know that AASs abuse exhibits several endocrine effects commonly include testicular atrophy, decreased fertility, gynecomastia, dyslipidemia, various forms of hepatotoxicity, neuropsychiatric disturbances besides variable increase in kidney functions tests (Almukhtar et al., 2015) to the point that androgen excess, (often 50–100 times its recommended physiologic levels), becomes an increasingly important cause of end stage renal disease (ESRD) (Kanayama et al., 2008). This could...
be attributed to podocyte apoptosis (Doublier et al., 2011). Focal segmental glomerular sclerosis (FSGS) is a pattern of glomerular injury caused by adaptive response to elevated glomerular capillary pressures and flow rates that are caused by increased body mass (D’Agati et al., 2004). This by time will lead to glomerular hypertrophy and soon become maladaptive, producing perihilar lesions of segmental sclerosis (D’Agati et al., 2004). Clinically, patients with maladaptive FSGS develop subnephrotic or nephrotic range proteinuria and they usually lack hypoalbuminemia and edema with reduced glomerular filtration rate (GFR) (Herlitz et al., 2010). Although patients with FSGS responded well to discontinuation of AASs use, weight loss, and the renin angiotensin system (RAS) blockade, others may progress to end stage renal disease (ESRD) (Herlitz et al., 2010).

From another point of view, for most athletes, sports nutritionists recommend a daily protein intake of 1.4–1.7 g/kg/day, (less than half of what is actually used by athletes nowadays) (Martin et al., 2005). Bodybuilders report high protein consumption, sometimes in excess of 500 g/d, with subsequent high metabolic burden (Herlitz et al., 2010). As regards to creatine consumption, There is substantial experimental and clinical data supporting the safety of creatine supplementation when it is used in the recommended amounts, but there is concern that excess dietary protein and creatine that is not accompanied by increased fluid intake may lead to a relative hypovolemia (Cooper et al., 2012). In the current study we asses and compare the effect of AASs and other nutritional supplements on kidney outcomes. We classified the 20 volunteers included in the research into 2 groups: Group 1: (steroid group) in which the volunteers use AASs (more than 2 years and less than 5 years) with concomitant use of whey protein, creatine monohydrate and branched chain amino acids intermittently for more than 2 years. Group 2: (non-steroid group) in which the volunteers use whey protein, creatine monohydrate and branched chain amino acids intermittently for more than 2 years.

In the current study, we demonstrated non-significant increase in S. Cr. in steroid group (group 1) (S. Cr: 1.76 ± 0.25). Besides non-significant increase in S. Cr. in steroid group (group 1) when we compare its level to non-steroid group (group 2) (S. Cr: 1.76 ± 0.25 vs. 1.57 ± 0.12). This was in agreement to (Almukhtar et al., 2015), who stated that long use of AASs could produce renal effects as variable elevations in serum creatinine and development of FSGS with subsequent substantial proteinuria. Sakemi et al., (1997) explained the potential effects of AASs on renal function by the direct toxic effect of androgens on glomerular cells that in turn will lead to mesangial matrix accumulation and podocyte depletion. From another point of view, McGuire et al., (2007) reported that androgens can induce oxidative stress and upregulate the components of renin angiotensin system (RAS) with its hazardous effect on renal functions. From another point of view, we demonstrated also non significant increase in S. Cr in the non steroid group (group 2) (S. Cr: 1.57 ± 0.12). This could be explained by (Woods, 1993) who stated that high protein consumption can cause an increase in renal blood flow and GFR in an adaptive response to the increase in nitrogenous wastes that are the byproduct of protein metabolism, and this process in turn may accelerate progression to glomerulosclerosis. Also, Almukhtar et al., (2015) reported cases of acute kidney injury in creatine users and this could be attributed to acute tubular necrosis. On the same side of view, Thorsteinsdottir et al., (2006) demonstrated other cases diagnosed as acute interstitial nephritis and explained this by presence of idiosyncratic allergic reactions. In our study, we demonstrated non significant increase in the amount of protein in 24 hours of collected urine (mg/24 hrs.) in steroid group (group 1) (24 hrs. urine ptn.: 859.50 ± 805.72). Also we noticed significant increase in the amount of protein in 24 hours of collected urine (mg/24 hrs.) in steroid group (group 1) when we compare its level to non steroid group (group 2) (24 hrs. urine ptn.: 859.50 ± 805.72 vs. 128.50 ± 48.25, p<0.001). This was in agreement with Almukhtar et al., (2015) who explained this by the hazardous effect of androgens on renal function with subsequent proteinuria due to development of FSGS. The mechanism of development of maladaptive forms of FSGS with increased body mass could be attributed to the structural and functional adaptations driven by increased hemodynamic stress on the glomerulus with podocyte depletion (D’Agati, 2008), which are unfortunately terminally differentiated cells and cannot proliferate. At that point, podocyte connections to the glomerular basement membrane (GBM) become mechanically strained and if these conditions persist, the podocytes eventually detach from the GBM, leading to development of a segmental scar (Kriz et al., 1998). From another point of view, we demonstrated also non significant increase in protein in 24 hours of collected urine in the non steroid group (group 2) (24 hrs. urine protein: 128.50 ± 48.25). Although there is no overt proteinuria, but still a pathological finding. This was in agreement with (Woods, 1993) who stated that the Nitrogenous wastes of protein metabolism could progress to glomerulosclerosis In contrast to this finding, Sandhu et al., (2002) reported that the renal adverse events in the users of creatine and protein supplement for muscle building, is small and usually associated with
exercise induced acute renal failure and rhabdomyolysis during intense training rather than the supplement effect. In the same side of view, Schwimmer et al., (2003), stated that renal pathology in highly muscular patients is rare. It well reported now that cessation of AASs is clearly the mainstay of treatment in cases of AASs associated toxicity. Additional treatment aimed at reducing hyperfiltration injury, such as RAS blockade along with lifestyle modification including reduction of strenuous exercise and weight loss, has been reported to help reduce proteinuria and stabilize renal function (Herlitz et al., 2010). No evidence supports the use of immunosuppressive therapies, including corticosteroids (Herlitz et al., 2010).

Conclusions
We should stress on the dangers of use of AASs for a long periods to achieve bodybuilding and increase the body performance on the renal functions. To add on, we also stress not to consume high protein and creatine supplements beyond the recommended dose that is reported by the sports nutritionists to keep normal renal functions.

References:

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