EFFECT OF TESTOSTERONE ON SERUM LIPOCALIN-2 IN ORCHIDECTOMIZED ADULT MALE ALBINO RATS

By

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ABSTRACT

Background: Lipocalin-2 (Lcn2) was initially identified as a protein secreted from human neutrophils. It has been implicated in many functions as inflammation, cell survival, innate immunity and biology of the genitourinary system as a developmental and a protective factor. The effect of testosterone on the circulating lipocalin-2 level in adult male rats is still unknown.

Objective: To explore the effect of testosterone on serum lipocalin-2 levels in orchidectomized adult male albino rats.

Material and Methods: The present study was conducted on 32 adult male albino Wistar rats divided into 4 equal groups: group (I): Sham operated control group; group (II): Orchidectomized group; group (III): Orchidectomized with subcutaneous physiologic testosterone replacement therapy; group (IV): Orchidectomized with subcutaneous supra-physiologic dose of testosterone.

Results: In group (II) and group (III), serum lipocalin-2 level significantly decreased compared to control group. In group (IV), there was further significant reduction in serum lipocalin-2 when compared with control group, group II and group III with a significant negative correlation with serum testosterone level.

Conclusion: Normal physiologic levels of testosterone are needed for normal lipocalin-2 expression. Disturbance of testosterone level (either by decrease or increase) significantly decreased lipocalin-2 level.

Key words: Lipocalin-2, orchidectomy, testosterone, lipid profile.

INTRODUCTION

Lipocalin-2 (Lcn2), also known as neutrophil gelatinase associated Lcn2 (Kjeldsen et al., 1993), was initially identified as a protein secreted from human neutrophils (Kjeldsen et al., 1994). In mice, multiple tissues can express Lcn2 including uterus, bone marrow, immune cells, liver, spleen, and kidney (Aigner et al., 2007).

Moreover, Lcn2 was identified as a new adipokine that is expressed and secreted by adipocytes, and it was reported to have a role in metabolism (Yan et al., 2007 and Zhang et al., 2008). It is also known to play a vital role in innate immunity and protect against bacterial infection (Kang et al., 2017).

Interestingly, testosterone is an anabolic hormone that affects body composition, body fat distribution (Marin et al., 1992), triglyceride and cholesterol levels (Phillips et al., 2003). Furthermore, low testosterone concentration may be considered a risk factor for the development of the metabolic syndrome in men as it may lead to central obesity and dyslipidemia (Laaksonen et al., 2004 and Muller et al., 2005).
However, the effect of orchidectomy on body fat distribution and development of metabolic syndrome in rats showed conflicting results (Varlamov et al., 2012).

Luque-Ramírez et al. (2013) and Martínez-García et al. (2013) have suggested that there are inter-connections between androgens and Lcn2. In rat studies, Nantermet et al. (2004) reported the presence of putative androgen response elements in the promoter regions of lipocalin encoding genes. Furthermore, Lcn2 influences the aromatase enzyme activity, which is considered a key enzyme of conversion of androgens to estrogen in adipose tissue and granulosa cells (Fried & Greenberg, 2012 and Guo et al., 2012).

To the best of our knowledge, no previous researches have studied the association between Lcn2 and serum testosterone level in adult male orchidectomized rats. However, several studies were done on the relation between Lcn2 and androgen in patients with polycystic ovary syndrome (PCOs) with clinical and/or biochemical signs of hyper-androgenism and their results were inconsistent.

As Diamanti-Kandarakis et al. (2008) and Gencer et al. (2014) found that lipocalin-2 concentrations were significantly lower in women with PCOS. On the other hand, Cakal et al. (2011) and Yılmazet al. (2017) found high Lcn2 levels in PCOS with no association with body fat percentage and were associated only with free testosterone.

So, the aim of this study was to clarify the possible effect of orchidectomy and testosterone replacement therapy on serum Lcn2 levels and lipid profile in orchidectomized adult male albino Wistar rats.

MATERIALS AND METHODS

Thirty two healthy adult male albino Wistar rats were used. Their weight ranged from 200-250 g. The rats were derived from the animal house, Faculty of Veterinary Medicine, Zagazig University. The rats were kept in steel wire cages (50×30×20 cm), 4 rats per cage. They were housed at standard conditions (25-30°C, natural dark/light cycle), and received food and water ad libitum. The animals were left to acclimatize for one week, then the animals were divided into 4 equal subgroups: control group (I): Rats were sham operated. Each rat received a daily dose of 0.2 ml/ 100g body weight sesame oil subcutaneously (sc); Group (II) (Orchi group): Rats were bilaterally orchidectomized then received daily dose of 0.2 ml/ 100g sesame oil subcutaneously (sc); Group (III) (Orchi +hormonal replacement): Rats were bilaterally orchidectomized then each rat received s.c. injection of physiologic dose of testosterone (0.3 mg/ 100g body weight dissolved in 0.2 ml sesame oil/ injection) given every other day (Staprans et al., 1999); Group (IV) (Orchi +supra-T): Rats were bilaterally orchidectomized then each rat received daily supra-physiologic doses of testosterone (3 mg/ 100g body weight dissolved in 0.2 ml sesame oil/ injection) (Jezek et al., 1993). Administration of drugs started one week after surgical procedures and continued for 14 days in all treatment groups.

Surgeries were performed after anesthetizing the rats with pentobarbital sodium (40 mg/kg) (Irahara et al., 2001). The
rats were placed in supine position. After shaving and sterilization of the skin of the scrotal area, the skin was incised, the tunica vaginalis was opened, and the testis and epididymis were removed after ligation of vas deference and scrotal blood vessels. Remaining tissues were returned to scrotal sac and incision was closed by non-absorbable sutures. The procedure was repeated on the other side. The same procedure was done in sham-operated rats without removal of the testis or epididymis (Foley, 2005).

Body mass index (BMI) was estimated according to the equation: body weight (g) /length² (cm) = BMI (g/cm²) (Novelli et al., 2007).

Blood collection: At the end of experimental period, animals were sacrificed, under light ether anesthesia after an over-night fasting, and blood samples (6-8 ml / rat) were obtained between 9-11 a.m. The serum was stored at -20°C until assayed.

Biochemical Analysis:

1. Serum Lcn2 levels according to Goetz et al. (2002) using rat Lcn2 enzyme-linked immunosorbent assay (ELISA) kit (Catalog Number: 201-11-5109, shanghai sunred biological technology, China).

2. Serum total cholesterol (TC) levels according to Allain et al. (1974) using rat cholesterol ELISA kit (Catalog Number: 2011-11-0198, shanghai sunred biological technology, China).

3. Serum triglycerides (TG) levels according to Naito (1989) using rat triglycerides ELISA kit (Catalog Number: 2011-11-0250, shanghai sunred biological technology, China).

4. Serum high density lipoproteins (HDL) levels according to Warnick et al. (1983) using rat HDL-cholesterol ELISA kit (Catalog Number: 2011-11-0255, shanghai sunred biological technology, China).

5. Serum low density lipoproteins (LDL) levels according to Friedwald et al. (1972) LDL was calculated as follows: LDL=TC-HDL-TG/5.

6. Serum testosterone levels according to Tietz (1998) using rat testosterone ELISA kit (Catalog Number: 2011-11-0183, shanghai sunred biological technology, China).

7. Serum follicular stimulating hormone (FSH) levels according to Rebar et al. (1982) using rat FSH ELISA kit (Catalog Number: 2011-11-0183, shanghai sunred biological technology, China).

8. Serum Luteinizing hormone (LH) levels according to Tietz (1985) using rat LH ELISA kit (Catalog Number: 2011-11-0180, shanghai sunred biological technology, China).

9. Serum tumor necrosis- α (TNF-α) according to Engelberts et al. (1991) by rat TNF–α ELISA kits (Elabscience Biotechnology, USA. Cat: EEL-H0109).

10. Serum interleukin- 1β (IL-1β) according to Yauoka et al. (2003) using the rat IL-1β Elisa kit (Bender Med System GmbH, Vienna, Austria).

Statistical analysis: The data obtained in the present study were expressed as mean ± SE for quantitative variables, one way ANOVA with LSD was done to compare means between groups. Pearson correlation was done (P value less than
0.05 was considered significant). The statistical analysis was done by using SPSS program (version 18 for windows) (SPSS Inc. Chicago, IL, USA.

RESULTS

Our results showed no significant difference in BMI among all groups (p>0.05). In group (II) and (III), there was a significant decrease in serum Lcn2 versus control group (p<0.01; p<0.05 respectively), while there was a non-significant change in serum Lcn2 between group (II) and group (III) (p>0.05). In group (IV), serum Lcn2 showed a significant decrease versus control group (p<0.001), group (II) (p<0.01) and group (III) (p<0.001); [Table 1, Fig 1].

![Figure 1: Serum Lcn2 in all groups.](image)

a: sig versus group I; b: sig versus group II; c: sig versus group III

Furthermore, serum testosterone significantly decreased in group (II) accompanied with significant increase in serum LH and FSH when compared with control group (p<0.001). In group (III), serum testosterone, LH and FSH showed insignificant difference compared to control (P>0.05). In group (IV), serum testosterone significantly increased, while serum LH and FSH significantly decreased. These changes were significant when compared to all groups (p<0.001) [Table 1].

Additionally, in group (II), there was no significant change in serum TG or HDL levels (p>0.05), while a significant increase was found in TC and LDL levels versus control (p<0.01; p<0.05; respectively). In contrast, group (III) showed a non-significant difference in TC, TG, LDL or HDL levels versus control (p>0.05). However, in group (IV), there was a significant increase in TC (p<0.001), TG (p<0.05), LDL (p<0.001) and a significant decrease in HDL (p>0.001) versus control [Table 2].

No significant difference was found in serum level of IL-1β and TNFα between group (I), (II) and (III) (p>0.05), but there was a significant decrease in serum levels of IL-1β and TNFα in group IV in comparison to other groups (p< 0.001) [Table 2].
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Table (1): Serum hormonal levels in all studied groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipocalin-2 (ng/ml)</td>
<td></td>
<td>60.6±3.82</td>
<td>48.78±2.52</td>
<td>52.01±2.38</td>
<td>34.71±2.46</td>
</tr>
<tr>
<td>Testosterone(ng/ml)</td>
<td></td>
<td>8.13±0.51</td>
<td>2.05±0.34</td>
<td>8.56±0.44</td>
<td>13.02±0.72</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td></td>
<td>14.22±0.79</td>
<td>22.52±1.06</td>
<td>13.6±0.71</td>
<td>8.63±0.6</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td></td>
<td>12.28±0.56</td>
<td>17.33±0.54</td>
<td>13.26±0.58</td>
<td>8.76±0.3</td>
</tr>
</tbody>
</table>

Table (2): Serum lipid profile and BMI in all studied groups

<table>
<thead>
<tr>
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<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mg/dl)</td>
<td></td>
<td>74.84±3.8</td>
<td>88.2±1.8</td>
<td>77.48±1.8</td>
<td>95.52±3.1</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td></td>
<td>104.81±6.2</td>
<td>116.26±7.8</td>
<td>101.55±4.5</td>
<td>129.1±8.05</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td></td>
<td>20.52±1.6</td>
<td>28.53±2</td>
<td>20.53±1.2</td>
<td>46.94±4.1</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td></td>
<td>37.49±1.8</td>
<td>36.41±1.6</td>
<td>36.71±1.9</td>
<td>22.76±3.5</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td></td>
<td>0.61±0.24</td>
<td>0.58±0.022</td>
<td>0.63±0.023</td>
<td>0.64±0.021</td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
<td></td>
<td>1.33±0.67</td>
<td>1.51±0.10</td>
<td>1.41±0.40</td>
<td>0.52±0.6</td>
</tr>
<tr>
<td>II-1β(pg/ml)</td>
<td></td>
<td>4.05±0.26</td>
<td>5.03±0.20</td>
<td>4.82±0.17</td>
<td>1.48±0.16</td>
</tr>
</tbody>
</table>

*: significant (p<0.05); a: versus (I); b: versus (II); c: versus (III)

No significant correlation was found between serum Lcn2 and BMI, serum TC, TG, LDL and HDL levels in groups (I, II, III) (p>0.05). However, there was a significant negative correlation between Lcn2 and TC, TG, LDL in group (IV) (P<0.01, p<0.05, p<0.05; respectively) [Table 3, Fig 7A,B,C], and there was a significant positive correlation between its level and HDL (p<0.05) in the same group [Table 3, Fig 7D].

A significant negative correlation was found between serum Lcn2 and serum testosterone in group (IV) (r=-0.781, p<0.05)[Table 3, Fig 4], while a positive correlation was found between serum Lcn2 and serum LH (r=0.713, p<0.05) and serum FSH in the same group (r=0.832, p<0.05) [Table 3]. A non-significant correlation was found between serum Lcn2 and testosterone in group (II) (r=0.379, p>0.05)[Fig 2] and (III), (r= -0.229, p>0.05) [Fig3].

Serum levels of Lcn2 correlated positively with IL-1β (p<0.01) and TNFα (p<0.001) in group IV (r=0.868, r= 0.958; respectively) [Fig 5&6].However, a non-significant correlation was found betweenLcn2 and IL-1β in group (I), (II) and (III) (r=0.143, 0.528 and 0.670; respectively). Moreover, a non-significant correlation was found betweenLcn2 and TNF-α in group (I), (II) and (III) (r=0.632, 0.337 and 0.616; respectively) [Table 3].
Table (3): Correlation between lipocalin-2 and measured biological parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>0.224</td>
<td>0.019</td>
<td>0.095</td>
<td>0.287</td>
</tr>
<tr>
<td>Testosterone (ng/ml)</td>
<td></td>
<td>0.206</td>
<td>0.379</td>
<td>-0.229</td>
<td>-0.781*</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td></td>
<td>0.131</td>
<td>-0.109</td>
<td>0.223</td>
<td>0.713*</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td></td>
<td>0.554</td>
<td>-0.135</td>
<td>0.104</td>
<td>0.832*</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td></td>
<td>-0.683</td>
<td>-0.035</td>
<td>0.206</td>
<td>-0.847**</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td></td>
<td>0.632</td>
<td>0.093</td>
<td>0.454</td>
<td>-0.736*</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td></td>
<td>-0.462</td>
<td>-0.318</td>
<td>0.469</td>
<td>-0.783*</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td></td>
<td>-0.187</td>
<td>0.255</td>
<td>-0.328</td>
<td>0.736*</td>
</tr>
<tr>
<td>IL-1β (pg/ml)</td>
<td></td>
<td>0.143</td>
<td>0.528</td>
<td>0.670</td>
<td>0.868**</td>
</tr>
<tr>
<td>TNFα (pg/ml)</td>
<td></td>
<td>0.632</td>
<td>0.337</td>
<td>0.616</td>
<td>0.958***</td>
</tr>
</tbody>
</table>

Figure (2): Correlation between serum lipocalin-2 and serum testosterone in group II.

Figure (3): Correlation between serum lipocalin-2 and serum testosterone in group III.
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**Figure (4):** Correlation between serum lipocalin-2 and serum testosterone in group IV.

**Figure (5):** Correlation between serum lipocalin-2 and IL-1β in group IV.

**Figure (6):** Correlation between serum lipocalin-2 and TNF-α in group IV.

**Figures (7 A, B, C, D):** Correlation between serum lipocalin-2 and lipid profile in group IV.

*significant: (p<0.05); **: (p<0.01); ***: (p<0.001).
DISCUSSION

Serum level of Lcn2 showed a significant reduction after orchidectomy. We expected an increase in serum Lcn2 level after orchidectomy because in human testosterone deficiency resulted in a state that includes certain criteria of metabolic syndrome (Laaksonen et al., 2004), like central obesity, dyslipidaemia, impaired glucose tolerance and insulin resistance (Muller et al., 2005 and Brand et al., 2014). These effects were attributed to an increase in body fat especially visceral fat (Clegg et al., 2003 and Christoffersen et al., 2006) which is one of the main sources of Lcn2 (Yan et al., 2007). However, in this study, there was no significant change in BMI of orchidectomized group versus control. This was in accordance with previous studies in rats which showed that orchidectomy in rats differs from human as it led to a decrease in food intake, percentage of lean body mass and an increase in fat percentage mainly in subcutaneous, but not visceral fat mass (Clegg et al., 2003 and Christoffersen et al., 2006). These reports about the change in body fat distribution following orchidectomy in rats might be partially responsible for the reduction in serum Lcn2.

Moreover, the reduction in Lcn2 level can also be explained by removal of the testis and epididymis during orchidectomy. Lcn2 protein was found to be expressed in male reproductive system as Lee et al. (2003) reported that Lcn2 mRNA is produced in both spermatogonial cells and Sertoli cells in the testis. In addition, Lcn2 is expressed in significant amounts in the caput of the epididymis bound to spermatozoa, and this expression was reported to be under androgen control (Suzuki et al., 2004 and Plant & Zeleznik, 2014). Interestingly, epididymal Lcn2 level increases by inflammatory stimuli that indicate a role for Lcn2 as a part of the innate immune response against bacterial infection in the epididymis (Flo et al., 2004 and Zhang et al., 2008). Furthermore, Lcn2 was reported to play a role in normal function of spermatozoa. Mouse Lcn2 delivers ferric iron to spermatozoa by internalization (Elangovan et al., 2004). It also enhances sperm motility by increasing pH inside the cell and elevating intracellular cAMP (Lee et al., 2003). These reports indicate a dual action of Lcn2 in the epididymis (Plant and Zeleznik, 2014).

The results also showed that hormonal replacement of rats with physiologic doses of testosterone caused slight elevation of serum Lcn2 versus control, but this increase did not reach statistical significance. Physiologic doses of testosterone following orchidectomy were associated with normal lipid profile versus control and may have caused normal fat distribution and improvement of metabolic disturbance caused by orchidectomy. These effects may result in this partial correction of serum Lcn2.

In the current study, we also noticed a further reduction of Lcn2 in group IV after administration of supra-physiologic dose of testosterone to orchidectomized rats. This reduction was significant compared to both group II and III. Moreover, serum levels of Lcn2 were negatively correlated with serum testosterone levels in this group. Our results were in line with those of Diamanti-
Kandarakis et al. (2008) who found low level of Lcn2 in PCOS patients with negative association with testosterone level.

This marked reduction in Lcn2 in this group might be attributed to the effect of supra-physiologic doses of testosterone on cytokine production, as our results showed that injecting orchidectomized rats with supra-physiologic doses of testosterone was associated with a significant decrease in serum levels of IL-1β and TNFα, and these levels were positively correlated with Lcn2. Previous studies reported that supra-physiological concentrations of testosterone suppresses pro-inflammatory cytokines and up-regulate anti-inflammatory cytokines as it attenuates the production of inflammatory cytokines such as TNFα, IL-1β (Corcoran et al., 2010 and Xu et al., 2015), and IL-6 (Vodo et al., 2013). IL-1β showed most profound effect on lcn2 expression and secretion in 3T3-L1 adipocytes (Zhang et al., 2014). Additionally, liver tissue was the most sensitive to TNFα treatment and resulted in an elevation of Lcn2 mRNA levels by more than 2000-folds (Zhao et al., 2014). So, the high level of testosterone in group IV might have decreased Lcn2 level by suppressing its production from the liver and adipose tissue through the inhibitory effect of testosterone on pro-inflammatory cytokines.

However, in our study, there was a non-significant change in IL-1β and TNF-α level between groups (I), (II) and (III) which was in line with those of Chin and Ima-Nirvana, (2017) who reported that the changes in these cytokine levels might not be significant enough to be detected in vivo.

In addition, McInnes et al. (2012) reported that androgen receptor activation in murine 3T3 adipocytes down-regulates retinol-binding protein 4 (RBP4) mRNA. Lcn2 belongs to the same lipocalin superfamily members of fatty acid binding proteins and retinol binding proteins with structural similarity (Lalonde et al., 1994). So, a similar effect of testosterone on lcn2 expression from adipocytes might be expected. Besides, high levels of testosterone can decrease adipose tissue mass which is one of the main sources of Lcn2. The absence of significant change in BMI in this group might be due to the anabolic effect of testosterone which increases lean body mass (muscle mass) with concomitant decrease in adipose tissue mass (Amsterdam et al., 2010).

Considering lipid profile, in orchidectomized group, serum levels of total cholesterol and LDL showed significant increase versus control. Physiologic doses of testosterone decreased these levels back to control group levels. These findings agreed with the results of previous cross-sectional studies which demonstrated an association between low serum testosterone and high total cholesterol and LDL-C levels (Barud et al., 2002 and Yao et al., 2011). Moreover, total cholesterol and LDL-C significantly increase in prostatic cancer patients receiving androgen deprivation therapy (ADT) (Braga-Basaria et al., 2006 and Yannucci et al., 2006). This effect may be due to decrease in activity of hepatic lipase (HL) and lipoprotein lipase (LPL) which depends on gonadal
hormones in its function (Tikkanen and Nikkila, 1987).

In addition, the increased total cholesterol in orchidectomized group may also be due to increase in acetyl CoA arising from an increase in β-oxidation of fatty acids, and acetyl CoA is a key substrate in the synthesis of cholesterol (Rang et al., 1995). Furthermore, LDL-C is the primary transporter of plasma cholesterol. So, the increase in LDL might be secondary to the increase in total cholesterol or reduction in LDL uptake by LDL receptor (PPAR-α and PPAR-γ) due to its down regulation by Low testosterone (Konstantinos and Christos, 2014).

However, in our study, no significant change was found in serum triglyceride or HDL-C in orchidectomized group, which was in line with the results of Kiel et al. (1989) and Denti et al. (2000) who found no association between level of serum lipids and endogenous testosterone. Others reported an increase in serum triglycerides and a decrease in HDL-C levels (Haffner et al., 1993).

Moreover, our results revealed significant elevation in total cholesterol, triglycerides, LDL and a significant reduction in HDL in group IV with injection of supra-physiologic doses of testosterone. This atherogenic lipid profile was previously described by Awad et al. (2012) when treated adult male albino rats with androgen anabolic steroids. Also, George (2003) and Gold et al. (2006) found an increase in triglycerides and total cholesterol level in androgen anabolic steroid (AAS) abusers. This effect of testosterone is induced mainly by induction of hepatic triglyceride lipase (HTGL) which is present in the luminal surface of hepatic endothelium and catabolizes HDL via its phospholipase activity (Awad et al., 2012). The activity of, HTGL has been reported to show a significant increase with androgen anabolic steroid therapy (Applebaum-Bowden et al., 1987). Besides, it was suggested that serum LDL levels may increase due to the induction of the enzyme HTGL and catabolism of very low density lipoprotein (Baldo-enzi et al., 1990).

Additionally, the results of this work showed a significant negative correlation between serum Lcn2 and TC, TG and LDL accompanied by a significant positive correlation with HDL in group (IV). These findings can be explained by the results of Paton et al. (2013) who reported that Lcn2 promotes total energy expenditure, lipid clearance and fatty acid oxidation via increased expression of genes involved in β-oxidation including peroxisome proliferator activated receptor-δ. So, the reduction in Lcn2 can affect lipid metabolism and participate in this atherogenic lipid profile.

Our results disagreed with those of De la Chesnaye et al. (2015) who demonstrated a decrease in Lcn2 level in patients with type 2 diabetes mellitus with no significant correlation between its levels and lipid profile, and suggested that the reduction in Lcn2 levels depend on the inflammation process through an unknown mechanism. Choi et al. (2008) also did not find any relationship between BMI, waist circumference, triglyceride, fasting glucose, and Lcn2 levels in patients with chronic heart disease. The conflicting reports about the correlation between Lcn2 and lipid profile may be
due to differences in species, study design, underlying disease, or feeding behavior.

**CONCLUSION**

Normal physiologic levels of testosterone are needed for normal lipocalin-2 expression. Disturbance of testosterone level (either by decrease or increase) significantly decreased lipocalin-2 level.

These findings highlight the possible association between serum Lcn2 and serum testosterone levels and the possible adverse effects of testosterone abuse on male fertility.

Further human studies are needed to clarify whether orchidectomy have a similar effect on serum lipocalin-2 in human or not, and to identify different hormonal and humeral factors affecting Lcn2 expression with more concentration on its impact on male reproductive function.

**REFERENCES**


تأثير التستستيرون على الليبوكلينات في مصل الدم في ذكور الجرذان البالغة المخصصة

مها عبد الحميد و نانيس المالكي
قسم الفسيولوجيا الطبية. كلية الطب. جامعة الزقاق

خلفية البحث: تم التعرف الأولي لهورمون الليبوكلينات كبروتين يفرز من خلايا الدم البيضاء المحاذية. وقد تدخل الليبوكلينات في كثير من الوظائف مثل الالتهاب ونجلة الخلايا و المناعة و الوظائف الحيوية للجهاز البولي والتناسلي، وقد عرف كعامل للتطور و الحماية. وتأثير هورمون التستستيرون على مستوى الليبوكلينات في ذكور الجرذان البالغة مازال غير معروف.

الهدف من البحث: دراسة تأثير التستستيرون على مستوى الليبوكلينات في ذكور الليبوكلينات في ذكور الجرذان البالغة بعد إزالة الخصيتين.

مواد و طرق البحث: تم استخدام 23 من ذكور الجرذان البالغة، وتم تقسيمهم إلى أربعة مجموعات متساوية كالتالي:

• المجموعة الأولى (الضبابية): تعرضت لفتح الجلد بمنطقة كيس الصفن دون المساس بالخصيتين.
• المجموعة الثانية: تم إزالة الخصيتين.
• المجموعة الثالثة: تم إزالة الخصيتين، ثم حقن الجرذان بهرمون التستستيرون بجرعة تحافظ على المستوى الطبيعي للهرمون في الدم.
• المجموعة الرابعة: تم إزالة الخصيتين، ثم حقن الجرذان بهرمون التستستيرون بجرعه عالية تحافظ على مستوى أعلى من المستوى الطبيعي للهرمون في الدم.

النتائج: حدث نقص ذو دلالة إحصائية في مستوى الليبوكلينات في الدم في المجموعة الثانية والثالثة بالمقارنة بالمجموعة الضبابية. وقد أوضحت النتائج حدوث نقص ذو دلالة إحصائية في مستوى الليبوكلينات بالمجموعة الرابعة عند مقارنتها بباقي المجموعات، مع وجود علاقة عكسية ذات دلالة إحصائية بين مستويات هورمون التستستيرون والليبوكلينات في نفس المجموعة.

الخلاصة: المستوى الطبيعي لهورمون التستستيرون مهم للحفاظ على مستوي طبيعي للليبوكلينات في الدم، وأي اضطراب في مستوى هورمون التستستيرون سواء بالزيادة أو النقص يؤدي إلى نقص في مستوى الليبوكلينات بالدم.