Role of Irisin Administration in Modulating Testicular Function in Adult Obese Albino Rats

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Abstract

Background: Irisin, exercise-induced myokine, is known to improve obesity-induced metabolic disturbances by enhancing thermogenesis and increasing energy expenditure. Recent studies have reported that irisin promoted cell proliferation and protected cells from apoptosis. However, the effects of irisin on testicular function in obese rats is still to be investigated.

Aim of the Study: This study was designed to explore the probable effects of irisin treatment on modulating the adverse effects of obesity on testicular functions with a trial to clarify some of the possible underlying mechanisms.

Material and Methods: Thirty adult male wistar albino rats (200±30g) were divided equally into 3 groups, group (I): Saline-vehicle treated normal fed group, group (II): Saline-vehicle treated rats were fed a High Fat Diet (HFD) for 10 weeks. Group (III): Irisin treated HFD-fed rats for 10 weeks and irisin was injected subcutaneously (150 µl daily for 4 weeks). Rats were weighed and serum levels of glucose, insulin, lipid profile, FSH, LH, estradiol & testosterone levels, epididymal sperm count and motility, testicular Malondialdehyde (MDA) level, Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GPX) activities, testicular and epididymal fat weights were estimated. Testicular histopathological study was done as well.

Results: There was a significant increase in the Body Mass Index (BMI) together with deterioration of metabolic, gonadal functions and testicular oxidant/antio-oxidant system in group (II), while exogenous irisin administration in group (III) resulted in: Significant decrease in BMI, insulin resistance with improvement in lipid profile, significant increase in serum FSH, LH & testosterone, sperm count and motility in male rats. Together with marked improvement in the testicular histoarchitecture. Additionally, there was a significant increase in testicular SOD, CAT & GPX activities. However, it significantly decreased testicular MDA level.

Conclusions: It could be suggested that irisin has a potential positive role against obesity-induced testicular dysfunction, which may be due to its role in maintenance of glucose & insulin homeostasis, its antioxidant properties and/or maintenance of gonadal hormonal function via indirect and/or direct effects on the gonads.

Key Words: Irisin – Obesity – Testicular function.

Introduction

OBESITY is a worldwide health problem that could lead to disturbance in both male and female fertility [1]. It has been reported that obesity can affect males fertility by decreasing the number of spermatozoids [2]. Furthermore, it has been seen that obese males frequently show a low testosterone (T) and a high estradiol levels [3]. Interestingly, this hormonal disturbance was found to be proportional to the degree of obesity [4]. Moreover, Insulin Resistance (IR) and Oxidative Stress (OS) could play a vital role in explaining how excess body fat interferes with the reproductive functions [1].

Irisin, a novel myokine secreted by skeletal muscle, has been first discovered and reported by Bostrom et al., [5]. It is synthesized by hydrolysis of fibronectin type III domain-containing protein 5 (FNDC5) [5]. Irisin has a critical role in improving insulin sensitivity and enhancing cognitive capacity during the regulation of obesity [6]. It causes over-expression of Uncoupling Protein-1 (UCP1) in adipose tissue resulting in the browning of white adipocytes participating in the treatment of obesity [7]. Despite irisin plays an important role in energy homeostasis, its biological actions on reproduction remain unclear [8,9].

As male factor can account for a high rate of infertility [10], the purpose of the present study was to assess the possible effect of irisin treatment on gonadal functions in obese adult male albino rats and to clarify some of the possible involved mechanisms.

Material and Methods

From 1st of October 2017 till the end of January 2018, thirty adult male wistar albino rats (weighing
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200±30g) were included in the present work after the approval of the Institutional Research Board of Faculty of Medicine-Zagazig University.

They were housed in room temperature and in natural dark/light cycles. They had free access to food and water. After a week of acclimatization, the animals were divided randomly into 3 equal groups:

Group (I): Control rats received standard diet (14% fat, 54% carbohydrate, 32% protein and 3.02 calories/g) for 10 weeks, Group (II): Rats received High Fat Diet (HFD) (Faculty of Agriculture, Zagazig University) (60% fat, 21% carbohydrate, 18% protein and 5.1 calories/g) for 10 weeks to induce obesity [11] and Group (III): The irisin treated rats; rats were fed HFD for 10 weeks and from the end of the 6th week till the end of the experimental period, irisin (Sigma-Aldrich) was injected in a daily dose of 12nmole/kg subcutaneously, each rat received 150 µl of prepared irisin solution in a concentration of 100ng/ml [12,13]. Rats in the control and obese untreated groups received saline simultaneously.

Calculating Body Mass Index (BMI): It can be used as an indicator of obesity where the cutoff value of obesity, BMI >0.68g/cm². BMI=body weight(g)/length² (cm²) [14].

Blood collection:

At the end of the intervention, the overnight fasting animals were sacrificed under light ether anesthesia, and blood samples were obtained by decapitation of all rats and were collected in clean plastic tubes for centrifugation. Serum was stored frozen at –20ºC until assayed.

1- Serum biochemical analysis:

A- Glucose level by spectrophotometer at 546nm according to Tietz [15] using glucose enzymatic (GOD-PAP)-liquizyme Kits. (Biotechnology, Egypt) and insulin level using rat insulin Enzyme-Linked Immunosorbtent Assay (ELISA) kit (RAB0904, Sigma-Aldrich Chemie GmbH, U.S.A) according to Starr et al., [16].

Calculation of homeostasis model assessment of IR (HOMA-IR)=Insulin (µU/mL) X glucose (mg/dl)/405 [17].


C- Total Cholesterol (TC), Triglyceride (TG) and High Density Lipoproteins (HDL) levels using the corresponding rat ELISA kit (Cat: 8-B-14002011-11-0255, 8-C-1150, BioSource Europe S.A.-Rue de l'Industrie, Nivelles-Belgium and 2011-11-0255, Shanghai Sunred biological technology, China; respectively) [18].

D- Low Density Lipoproteins (LDL) levels was calculated as follows: LDL=TC-HDL-TG/5 [19].

2- Testicular examination:

Midline incision along the abdominal wall was done, the testes were quickly removed, washed in cold physiologic saline, and were dried with filter paper. The weight of the right testes were measured using an electronic balance, then they were processed for histopathological studies and the left one was homogenised for biochemical estimations of oxidant/antioxidant enzyme activities.

- Preparation of testis homogenate: The testes were sliced and homogenized in cold 50mM phosphate buffer (pH 7.0) containing 0.1mM EDTA to give 10% homogenate (w/v). The homogenates were centrifuged at 1000r.p.m. for 10min. The supernatants were separated and used for enzymes activity assays and lipid peroxidation determination [20].

- Testicular antioxidant system evaluation: Assay of Superoxide Dismutase (SOD) activity according to the method described by Kakkar et al., [21], assay of Catalase (CAT) activity according to the method described by Luck [22], assay of Glutathione Peroxidase (GPx) activity according to the method described by Reddy et al., [23] and assay of Malondialdehyde (MDA) level according to the method described by Ohkawa et al., [24] using spectrophotometer at 560nm, 240nm, 430nm and 535nm; respectively (Germany).

- Testicular histopathological examination: Testes were then fixed in 10% formaldehyde in fresh alcoholic bouin's fluid for 8 hours, and then processed and embedded in paraffin wax, sectioned at 5 µm thickness, and stained in hematoxylin-eosin. The sections were examined under a light microscope and the general histological appearance was assessed [25].

3- Spermat parameters analysis: The right epididymis of each rat was dissected, removed and minced in 2ml of Hank's buffer salt solution at 37°C [26]. After 5min incubation at 37°C, the cauda epididymis sperm count was analyzed using the standard hemocytometric method. The percentage of sperm motility was calculated.
using the number of live sperm cells over the total number of sperm cells [27].

Statistical analysis: Statistical tests were performed using the Statistical Package for Social Sciences (SPSS), Version 18.0 (SPSS, Chicago, IL, USA) for Windows 7. All data are expressed as the means ± Standard Error of the Mean (S.E.M). Multiple groups comparisons were carried using one-way ANOVA, followed by post hoc test, and p<0.05 was considered to be statistically significant.

Results

The present study showed that HFD induced significant increase in BMI, serum glucose, insulin and calculated HOMA-IR (p<0.001) in group (II) when compared with control group. Moreover, there was a significant increase in serum TC, TG, LDL (p<0.001) with a significant decrease in serum HDL (p<0.01) in the same group in comparison to control group.

In addition, treatment of obese rat with exogenous irisin led to a significant decrease in BMI, glucose, insulin, HOMA-IR, TC, TG, LDL (p<0.001) when compared to group (II). However, these parameters were significantly increased when compared with control group (p<0.001), accompanied with a significant increase in HDL (p<0.01) when compared with group (II), while, this change was insignificant when compared with control group (p>0.05) (Table 1).

Table (1): Metabolic parameters in all groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (g/cm²)</td>
<td>0.52±0.01</td>
<td>0.81±0.02</td>
<td>0.63±0.02</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>86.8±2.08</td>
<td>216.9±8.16</td>
<td>147.6±6.54</td>
</tr>
<tr>
<td>Insulin (μIU/ml)</td>
<td>14.5±0.58</td>
<td>30.3±0.94</td>
<td>18.4±0.64</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>3.08±0.07</td>
<td>16.35±1.03</td>
<td>6.65±0.25</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>95.25±1.81</td>
<td>191.1±4.89</td>
<td>155.8±2.59</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>55.1±2.62</td>
<td>108.1±2.37</td>
<td>78.6±2.40</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>66.98±1.39</td>
<td>156.1±6.63</td>
<td>122.98±1.74</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>17.2±0.99</td>
<td>13.35±2.68</td>
<td>17.1±0.78</td>
</tr>
</tbody>
</table>

*: Sig vs. group (I).
#: Sig vs. group (II).

As regard to serum hormonal profile, our results showed a significant reduction in FSH (p<0.001), LH (p<0.01) and T (p<0.001) levels accompanied by a significant increase in E2 (p<0.001) level in group (II) when compared with control group. However, treatment of obese rats with exogenous irisin in group (III) revealed a significant increase in FSH (p<0.001), LH (p<0.05) and T (p<0.001) levels with a significant decrease in E2 (p<0.001) level in comparison to those of group (II).

In addition, serum T was significantly low in irisin-treated group when compared with control group (p<0.05). However, serum E2 was significantly high in the same group in comparison to control group (p<0.001). While, there was an insignificant change in FSH and LH after treatment with irisin in group (III) in comparison to control group (p>0.05) (Table 2).

Table (2): Serum FSH, LH, T, E2 levels, right testicular, epididymal fat weights, sperm count and motility of all studied groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH (μIU/ml)</td>
<td>0.33±0.22</td>
<td>0.16±0.01</td>
<td>0.29±0.02</td>
<td></td>
</tr>
<tr>
<td>LH (μIU/ml)</td>
<td>1.5±0.12</td>
<td>1.03±0.07</td>
<td>1.3±0.14</td>
<td></td>
</tr>
<tr>
<td>T (ng/ml)</td>
<td>4.2±0.28</td>
<td>1.8±0.13</td>
<td>3.5±0.13</td>
<td></td>
</tr>
<tr>
<td>E2 (Pg/ml)</td>
<td>5.7±0.35</td>
<td>12.1±0.60</td>
<td>8.1±0.40</td>
<td></td>
</tr>
<tr>
<td>Testicular weight (g)</td>
<td>1.65±0.27</td>
<td>0.9±0.71</td>
<td>1.42±0.79</td>
<td></td>
</tr>
<tr>
<td>Epididymal fat weights (g)</td>
<td>3.8±0.15</td>
<td>5.7±0.17</td>
<td>4.4±0.14</td>
<td></td>
</tr>
<tr>
<td>Sperm count (million/mm³)</td>
<td>53.4±1.53</td>
<td>20.9±0.8</td>
<td>38.8±0.69</td>
<td></td>
</tr>
<tr>
<td>Sperm motility (%)</td>
<td>76±1.18</td>
<td>25.9±1.44</td>
<td>54.5±1.57</td>
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</table>

*: Sig vs. group (I).
#: Sig vs. group (II).

Moreover, our results showed a significant increase in epididymal fat weight (p<0.001) accompanied by significant decrease in testicular weight (Table 2), epididymal sperm count and motility (p<0.001) in HFD-fed rats in comparison to control group. Interestingly, irisin treatment caused a significant reduction in epididymal fat weights (p<0.001) together with a significant increase in testicular weight (Table 2), epididymal sperm count and motility (p<0.001) in group (III) when compared with group (II) (Table 2).

However, there was a significant increase in epididymal fat weights (p<0.05) accompanied by a significant decrease in epididymal sperm count and motility (p<0.001) in group (III) when compared with group (I). While, there was an insignificant change in testicular weight between both groups (p>0.05) (Table 2).

Table (3): Testicular oxidant and anti-oxidant enzymes level in all groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (nmol/gm tissue)</td>
<td>113±1.53</td>
<td>194±2.88</td>
<td>128.6±1.38</td>
<td></td>
</tr>
<tr>
<td>SOD activity (U/mg protein)</td>
<td>73.6±3.8</td>
<td>35.3±2.19</td>
<td>65.3±1.81</td>
<td></td>
</tr>
<tr>
<td>CAT activity (U/mg protein)</td>
<td>19.0±0.82</td>
<td>7.85±0.36</td>
<td>16.7±0.40</td>
<td></td>
</tr>
<tr>
<td>GPX activity (U/mg protein)</td>
<td>24.5±0.64</td>
<td>14.5±0.62</td>
<td>22.0±0.82</td>
<td></td>
</tr>
</tbody>
</table>

*: Sig vs. group (I).
#: Sig vs. group (II).

Considering oxidant/antioxidant enzymes, the result of the present work showed a significant increase in testicular MDA level with a significant reduction in testicular SOD, CAT and GP X activity.
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(\(p<0.001\)) in HFD-fed rats in comparison to control group (Table 3).

However, irisin treatment significantly reduced testicular MDA level (\(p<0.001\)) which was accompanied with a significant elevation in testicular SOD, CAT and GPX activity (\(p<0.001\)) in group (III) when compared with group (II). Additionally, in group (III) testicular MDA level was significantly elevated (\(p<0.001\)) when compared with group (I).

While, testicular SOD, CAT activity were significantly lowered than those of group (I) (\(p<0.05\) and \(p<0.01\); respectively) with an insignificant change in testicular GPX activity between the same groups (\(p>0.05\)) (Table 3).

In respect to the histopathological studies, testicular sections in HFD-fed rats showed atrophy in the walls of seminiferous tubules with reduction of sperm Lineage cells. Moreover, walls of tubules showed destruction of sertoli cells with increased thickness of the basement membrane Fig. (2). However, exogenous irisin treatment in group (III) induced a marked improvement in testicular histotarchitecture Fig. (3).

Discussion

Previous studies have shown a direct relationship between obesity and infertility with an association between metabolic disturbances and hormonal dysregulation \([1,28]\).

After its discovery in 2012, irisin, a novel myocytokine was given a great therapeutic potential for the treatment of obesity and metabolic syndrome \([5]\). Recently, irisin was reported to regulate body weight, insulin sensitivity, and glucose homeostasis \([29]\). So it may be helpful in management of detrimental effect of obesity on testicular function.

The results of the present study revealed that HFD feeding of rats for 10 weeks resulted in a significant increase in BMI, blood glucose, insulin and HOMA-IR when compared with that of control rats which realized the successful establishment of a rat model of obesity with IR.

Moreover, our results revealed that, HFD-induced obesity had negatively alter testicular function in adult rats, as we reported a significant reduction in serum levels of LH, FSH, T, and elevation of serum E2 levels accompanied by marked reduction in epididymal sperm count and motility together with a significant decrease in testicular weight, and a significant increase in epididymal fat, in addition to atrophy in the walls of seminiferous tubules, reduction of sperm Lineage cells, destruction of sertoli cells and increased thickness of the basement membrane in the histopathological studies of testicular sections in HFD group when compared with control group. These findings are supported by the findings of other investigators in both animals and humans \([30,31]\).

Interestingly, in case of obesity increased conversion of T to estradiol in the adipose tissue might contribute to decreased plasma T concentrations
leading to secondary hypogonadism [32]. In addition, as estrogen receptors are present in hypothalamic nuclei and pituitary gonadotropes, so increased circulating E2 level leads to suppression of the hypothalamic-pituitary axis affecting gonadotrophin releasing hormone (GnRH) pulsing and resulting in subclinical hypogonadotropic hypogonadism [33]. Other authors also suggested that estradiol could have a direct effect on testicular environment altering spermatogenesis via degeneration of Leydig cells [34].

It is worth saying that insulin is considered an important factor that plays a regulatory role in reproductive function as GnRH-expressing neurons can increase the expression of GnRH in response to insulin stimulation via insulin receptors by increasing in the expression of the transcriptional factor (c-fos) [35]. However, it has been suggested that obese patients with IR have a diminished sensitivity to insulin action in the hypothalamo-pituitary-gonadal axis altering GnRH release which subsequently impair testicular steroidogenesis leading to decreased circulating T concentrations [36], which provides an evidence that high insulin levels with IR may play an important role in infertility in obese males [37].

The present study showed that exogenous irisin improved spermatogenic activity, in the form of significant increase in sperm count and motility together with a significant increase in testicular weight and decrease in epididymal fat weight. Moreover, it caused improvement in hormonal profile, in addition, our findings are Supported by the marked improvement in testicular histomorphology in group (III) in comparison to obese non treated rats.

The present study tried to explain the possible involved mechanisms through which irisin improved the spermatogenic activity. It was noticed that irisin decreased BMI and IR as proved by significant reduction in serum glucose, insulin and HOMA-IR in group (III) in comparison to group (II) which was in line with the observations of Xin et al., [38] who suggested that irisin can reduce IR by increasing glucose uptake accompanied with reduced gluconeogenesis in the liver.

Furthermore, it could also increase acetyl-CoA carboxylase-1 phosphorylation in skeletal muscle increasing fatty acid oxidation, along with an increase in mitochondrial Ucp1 expression in the epididymal adipose tissue leading to increase in energy expenditure, oxygen consumption and enhancing basal metabolism via browning of white adipose tissue [38].

Moreover, mitogen-activated protein kinase (AMPK) in skeletal muscle is an important regulatory molecule for lipid metabolism, as the increase in their phosphorylation can improve glucose intake and energy metabolism in the body [39]. Interestingly, Lee et al., [40] reported that irisin can activate AMPK in skeletal muscle, promoting fatty acid oxidation, and alleviate the occurrence of metabolic disorders. Additionally, Hou et al., [41] noticed that treatment of HFD mice with irisin increased adiponectin significantly, which is known to improve insulin sensitivity by increasing fatty acid oxidation and energy expenditure [42].

Additionally, in animal studies, researchers suggested a link between dyslipidemia and infertility, as they reported that hypertriglyceridemia and high cholesterol may decrease sperm acrosome reaction kinetics, and Leydig and Sertoli cell secretory capacity [43,44]. In the present study, irisin treatment decreased total cholesterol, LDL and total triglycerides, these findings were in line with what reported by Oelmann et al., [45] who noticed that an improved lipid profile in association with irisin. As there were inverse associations between irisin concentrations and total, LDL cholesterol as well as triglycerides. Providing another mechanism by which irisin molecule could improve testicular function in obese subjects.

In addition, irisin may improve hormonal profile through a direct stimulatory effect on GnRH release, this was reported by the observation of Jiang et al., [8] who noticed that irisin may serve as a novel intra-pituitary factor maintaining gonadotropins gene expression and increasing their mRNA levels, providing another mechanism for improving testicular function in this work.

Furthermore, our results showed a significant elevation in the testicular MDA level accompanied with a significant reduction of testicular antioxidant enzymes CAT, SOD and GPX activities in obese rats (group II) in comparison to control group, it was noted that excess adiposity is associated with systemic pro-inflammatory state [46], increased OS and Reactive Oxygen Species (ROS) production [47].

Interestingly, it was established also that hyperglycemia elicits an increase in ROS production [48]. As testicular tissues are highly rich in polyunsaturated fatty acid content of sperm membranes, testicular tissues and spermatozoa are very sensitive to ROS attack and lipid peroxidation [49]. Moreover, Henkel [50] explained OS in the epididymis by excess fat deposition in the heads of the epididy-
midis, with reduction in the antioxidant system which leads to increased free radicals production that could induce genotoxicity by initiating sperm DNA denaturation and fragmentation and limiting DNA repair [51].

Additionally, Ibrahim et al., [52] noticed the increased apoptosis mediated by OS in the epididymis of obese rats could have an impact on the epididymal function, resulting in a low sperm count, viability and motility.

In the present study, rats treated with irisin showed reduced OS state that was proved by the significant reduction in MDA and increase in testicular antioxidant enzymes CAT, SOD and GSH activities in comparison to obese non treated rats. In line with our findings, irisin was suggested to have antioxidant role as it was reported to increase the expression of antioxidant enzymes in vascular endothelial cells [53] and pancreatic β cells [54] by inhibiting OS-induced activation of the Protein kinase C-β/nicotinamide adenine dinucleotide phosphate oxidase (PKC-β/NADPH) and nuclear factor kappa-β/inducible Nitric oxide synthase (NF-κB/iNOS) signaling pathways in high glucose/ high fat fed rats.

It is worth saying that OS stimulates cytokines secretion as interleukin-1 β and tumour necrosis factor-α (TNF-α) by macrophages and other inflammatory cells which affect both steroidogenesis and spermatogenesis [55]. Interestingly, Hou et al., [41] and Mazur-Bialy et al., [56] noticed that irisin has a significant suppressive effect on NF kB activity and suggested that irisin may have an anti-inflammatory effect, counteracting inflammatory cytokines such TNF as and interleukins.

Moreover, we suggested that irisin could possibly protect the testicular germ cells against the adverse effects of obesity and accelerates testicular regenerative processes in this condition via its important role in the down-regulation the proapoptotic proteins and up-regulation of the antiapoptotic proteins [54,57].

Furthermore, another possible mechanism by which irisin could enhance the rate of total sperm motility is its ability to increase intracellular Ca²⁺ [58], as Marquez et al., [59] stated that elevation of intracellular Ca²⁺ can hyperactivate sperm motility which is essential for fertilization.

Conclusion:

Irisin may have a protective effect against HFD-induced testicular damage as treatment of obese rats with irisin can reverse these detrimental effects by improving spermatogenesis and steroidogenesis possibly due to its direct and/or indirect beneficial effects on insulin resistance, Oxidative stress and hypophyseal-testicular hormonal axis providing a new approaches for the treatment of metabolic and reproductive disorders complicating obesity.

Further studies are needed to validate the mechanisms of irisin signaling pathway on testicular spermatogenic function.

Acknowledgement:

To Professor/Hayam Rashid, Pathology Department, Faculty of Medicine, Zagazig University for performing testicular histopathological studies.

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دور الإيبرسين في تعديل وظائف الخصية
في الجرذان البيضاء المصابة بالسمنة

المقدمة: الإيبرسين هرمون يفرز من خلايا العضلات وباكر على تنظيم العديد من المسارين السريرولوجية والمتقابل الغذائي. وقد أثبت بعض الدراسات قدرة الإيبرسين على تقليل موت الخلايا المرقب ولكن تأثير هذا الهرمون على وظائف الخصية في ذكر الجرذان المصابة بالسمنة يحتاج إلى دراسة.

الهدف من الدراسة: سمحت هذه الدراسة لتوضيح الدور المحتمل للعلاج بالإيبرسين لتحسين الأضرار المصاحبة للسمنة على وظائف الخصية في محاولة لتوضيح بعض الطرق التي يمكن إبرسين من خلالها تحقيق هذا التأثير في ذكر الجرذان البيضاء البالغة.

مواقد وطرق البحث: قد تم إعداد ثلاثين من ذكور الجرذان البيضاء البالغة (400-450 جم) وقد قسمت عشوائياً إلى ثلاث مجموعات متساوية كاثلثية: المجموعة الأولى: المجموعة الضابطة وقد تغذت بها الجرذان على الغذاء المعتاد، المجموعة الثانية: وقد تغذت فيها الجرذان على غذاء عائلي الدهن لمدة 10 أسابيع، المجموعة الثالثة: وتغذت الجرذان على غذاء عائلي الدهن، ثم حققتها بالإيبرسين تحت الجلد لمدة أربعة أسابيع.

وهي نتائج الدراسة:
1- تم وزن الجرذان وقياس مستوى السكر والأنسولين والدهون وFSH واللوكتيتين والإستراديل والإستربيلستروين في محل الدم، كما تم تقييم نموذج التوازن لمؤشر مقاومة الأنسولين (هوما-إن)

2- بالإضافة إلى تغييرات الخصية ووزن الدهن المحكيطة بالبربخ مع حساب عدد الخلايا المنوية بنسبة الحياة بها في عينة من منى البربخ.

3- وقد تم أيضا قياس إنزيمات الأكسدة ومضادات الأكسدة في ناقص الخصية ود.الالواحدية وفوق الأكسيد الديمسيلات والكاليت وبروكسيد الجليكليتين.

4- وقد تم عمل معاطف مستوية للخصية في الجرذان لكل مجموعات الدراسة.

النتيجة: لقد أثبتت الدراسة أن العلاج بالإيبرسين أدى إلى وجود تحسين ذات دالة إحصائية وزن الجرذان ومقدار الأنسولين مع تحسن ذات دالة إحصائية في نسبة دهون الدم في المجموعة البالغة للجربين في المجموعة الثانية. بالإضافة إلى ذلك لذي العلاج بالإيبرسين واللوكتين والاسترويديلان وعدد ونسبة حركة الخلايا المنوية مع تحسين في مستوى FSH واللوكتيتين والإستربيلستروين بعد ونسبة حركة الخلايا المنوية مع تحسين في مستوى الإستراديلون في نفس المجموعة بالمقارنة بالمجموعة الثانية. وقد وجد زيادة ذات دالة إحصائية في مستوى إنزيمات مضادات الأكسدة مع تحسين في إنزيمات الأكسدة في ناقص الخصية ود.الالواحدية وأخذ الدراسات المستوية للخصية هذا التحسن في تركيب الأنسجة والخلايا للجرذان.

الخلاصة: يمكن أن يكون أولئك الإيبرسين هرمون دور إيجابي ضد الأضرار المضادة للسمنة على وظائف وتكوين الخصية. وقد يكون هذا التأثير نتيجة لدورة هذا الهرمون على ضبط نسبة السكر والانسولين بالدم بالإضافة إلى تقليل الأكسدة في ناقص الخصية كما أن الإيبرسين له القدرة على تنظيم هورمونات الدف التحسينية بطريقة مباشرة أو غير مباشرة.