SERUM NESFATIN-1 LEVELS IN RAT MODEL OF NON-ALCOHOLIC FATTY LIVER DISEASE

By

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is a frequent progressive disorder manifested by fat accumulation in the liver and usually related to obesity and insulin resistance, but its pathogenesis is still uncertain. Nesfatin-1 is a polypeptide derived from nucleobindin-2 and involved in regulation of food intake and glucose homeostasis. The relationship between nesfatin-1 and NAFLD is still controversial.

Objective: To evaluate serum levels of nesfatin-1 in NAFLD model induced by high fat diet (HFD) in male albino rats.

Material and methods: Forty eight male adult albino rats were divided into four equal groups: 2 control groups that were fed ordinary diet for 4 weeks (group IA) and 12 weeks (group IB), and 2 HFD groups that were fed HFD for 4 weeks (group IIA) and 12 weeks (group IIB). In all groups, abdominal circumference, body weight, serum levels of nesfatin-1, insulin, glucose, C-reactive protein (CRP), lipid profile parameters, and liver enzymes (ALT & AST) were measured. BMI and HOMA-IR were calculated, and isolated liver tissues were examined histopathologically.

Results: After 4-week and 12-week-HFD feeding, the rats developed simple steatosis and steatohepatitis, respectively. These were proved by the progressive rise of liver enzymes and the histopathological findings. Besides, there was a significant progressive rise in BMI, HOMA-IR, serum levels of nesfatin-1, glucose, insulin, CRP, and all lipid profile parameters except high density lipoprotein that significantly decreased in HFD groups in comparison to control groups. Moreover, nesfatin-1 correlated positively with all measured parameters in HFD groups except for HDL that showed negative correlation with nesfatin-1.

Conclusion: Serum levels of nesfatin-1 increased in NAFLD rat model induced by HFD. This rise may be attributed to feeding rats with HFD, hyperglycemia or may compensate for the inflammation and disturbed metabolism.

Key words: NAFLD, nesfatin-1, lipid profile, HOMA-IR.

INTRODUCTION

NAFLD, defined by the presence of fat in the liver in absence of alcohol consumption, is a wide clinico-pathological disease that ranges from simple steatosis to steatohepatitis through to fibrosis and even cirrhosis (Targher et
A strong association was reported between NAFLD and metabolic disturbances such as insulin resistance, dyslipidemia, diabetes mellitus, and central abdominal obesity (Katsiki et al., 2016). NAFLD was considered as an independent risk factor for cardiovascular diseases, and liver-related and extra hepatic-related mortalities (Dunn et al., 2008 and Soderberg et al., 2010). The increased prevalence of NAFLD might be attributed to the increased frequency of obesity and diabetes in the general population (López-Velázquez et al., 2014).

Nesfatin-1 is an 82–amino acid polypeptide that is widely expressed in the brain and several peripheral tissues (Stengel et al., 2009). Several effects of nesfatin-1 were reported including anorexia and reduction of body weight (Stengel and Taché, 2010), regulation of glucose and lipid metabolism and insulin sensitivity (Zhang et al., 2012 and Shimizu & Osaki, 2013), in addition to the anti-inflammatory and anti-apoptotic properties (Zsavc? et al., 2011).

Few and contradictory data were found about the relationship between circulating levels of nesfatin-1 and NAFLD. While Basar et al. (2012) reported reduced serum levels of nesfatin-1 in patients having NAFLD, another study revealed increased plasma levels of nesfatin-1 in rat model of NAFLD (Wu et al., 2016).

The aim of the present work was to evaluate serum levels of nesfatin-1 in NAFLD model induced in adult male albino rats by HFD and to find out the possible correlation to some glycemic, metabolic and inflammatory parameters.

**MATERIAL AND METHODS**

The study was carried out on 48 adult healthy male albino rats of a local strain weighing 180-200 g that were purchased from the animal house, Faculty of Veterinary Medicine, Zagazig University. Rats were kept at room temperature, housed 4 animals per cage in steel wire cages (50 cm x 60 cm x 60 cm) under hygienic conditions, kept on a normal light/dark cycle, had free access to water and received care along the lines of the national health guidelines. The experimental procedures were applied in the animal house, Faculty of Medicine, Zagazig University and were accepted by the Institutional Research Board, Faculty of Medicine, Zagazig University.

After acclimation for one week, the rats were divided into 2 major equal groups: **Control group (I)** (n=24); that was subdivided equally into 2 subgroups (IA and IB); where rats were fed standard diet (12.6 kJ/g; 5% fat, 18 % protein and 77% carbohydrate) for 4 weeks and 12 weeks, respectively, and **HFD-fed group (II)** (n=24): that was subdivided equally into 2 subgroups (IIA and IIB); where rats were fed HFD (23.4 kJ/g; 58 % fat, 18% protein and 24% carbohydrate) for 4 weeks (for induction of steatosis) and 12 weeks (for induction of non-alcoholic steatohepatitis;
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NASH), respectively (Zhang et al., 2010).

The following anthropometric parameters were measured: Body weight (BW) was recorded at the start and the end of the experiment, rat nose to anus length was measured according to Warnick et al. (1983) and abdominal circumference (AC) was measured according to Gerbaix et al. (2010). BMI index was calculated according to Novelli et al. (2007) equation [body weight (g)/length² (cm²)]. Obesity was considered when BMI exceeds 0.68 gm/cm².

Blood collection: Rats were anesthetized using ether at the end of the experiment after overnight fasting, and blood was obtained from all rats by decapitation and collected in plastic centrifuge tubes. Blood was centrifuged for 15 minutes at 3000 r.p.m. and serum was separated and stored at -20°C until used for measurement of the following parameters: Nesfatin-1 levels were measured using rat Nesfatin-1 ELISA Kits (Shanghai Sunred biological technology, China) according to Basar et al. (2012). Glucose levels were measured using enzymatic (GOD-PAP)-liquizyme glucose kits (Biotechnology, Egypt), according to Tietz (1995). Insulin levels were measured using KAP1251-INS-EASIA (Enzyme Amplified Sensitivity Immunoassay) rat Kits (BioSource Europe S.A., Belgium) according to Temple et al. (1992). Calculation of the homeostasis model assessment of insulin resistance (HOMA-IR) was done using the following equation: [fasting serum insulin (µIU/mL) x fasting serum glucose (mg/dl)/405] according to Matthews et al. (1985). Total cholesterol (TC) levels were measured using rat total cholesterol kits (BioSource, Europe S.A), according to Tietz (1995). Triglycerides (TG) levels were measured using triglycerides ESPAS SL kits A (Eltech S.A., Lyon, France) according to Naito (1989). High density lipoproteins (HDL) levels were measured by using rat HDL kits (Catalog Number: 2011-11-0255, Shanghai Sunred biological technology, China) according to Nauk et al. (1997). Low density lipoproteins (LDL) levels were calculated using the following equation: LDL = TC-HDL-(TG/5) according to Friedwald et al. (1972). Very low density lipoproteins (VLDL) levels were calculated according to the equation: VLDL = TG/5 (Tietz, 1995). Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) levels were measured using rat ALT and AST ELISA kits (Catalog Number: 2011-11-0595, Shanghai Sunred biological technology, China), according to Rec (1970). C-reactive protein (CRP) levels were measured according to Kimberly et al. (2003) using rat immuno assay kits (Monobind Inc Lake Forest, USA).

Histopathological examination of liver: The isolated liver tissues were fixed for 48-60 hours in 10% buffered formalin solution, then processed through ethyl alcohol and xylene series, and after that embedded in paraffin blocks. Sections
with 5μm thickness were made from liver specimens, and then stained with hematoxylin and eosin according to Altunkaynak (2005). The stained samples were evaluated using light microscope.

**Statistical analysis:** Results were presented as mean ± SD. Statistical analysis was performed using SPSS program, version 19 (SPSS Inc., Chicago, IL, USA). One way Analysis Of Variance (ANOVA) followed by LSD post hoc test was used to compare statistical differences between the groups. Besides, Pearson’s correlation was used to analyze correlations between serum levels of nesfatin-1 and the measured parameters. P value <0.05 was considered significant for all performed statistical tests.

**RESULTS**

There was a statistically significant and progressive rise in final BW, BMI and AC in 4-week-HFD group and 12-week-HFD group (IIA and IIB) in comparison to their time-corresponding control groups (IA and IB). There was also a statistically significant and progressive elevation in serum levels of glucose, insulin and HOMA-IR index in HFD groups compared with their time-matching control groups. Concerning the lipid profile parameters, there was a significant progressive increase in serum levels of TC, TG, LDL and VLDL, while there was a significant progressive decrease in serum HDL levels in HFD groups in comparison to their time-equivalent control groups. As regard the liver enzymes, there was a statistically significant and progressive increase in serum levels of ALT and AST in the HFD groups in comparison to their time-matching control groups. Moreover, there was a significant progressive increase in the serum levels of the inflammatory marker; CRP in HFD groups compared with control groups. Serum nesfatin-1 levels significantly increased in 4-week-HFD group and more markedly increased in 12-week-HFD group in comparison to their time-matching control groups. No statistically significant changes were found in serum levels of all measured parameters in 12-week control group compared with 4-week control group except for the final body weight (Table 1).

Statistically significant positive correlations were found between nesfatin-1 and all measured parameters in 4-week and 12-week-HFD groups, except HDL which showed a significant negative correlation with nesfatin-1. No significant correlations were found between serum levels of nesfatin-1 and the other parameters in control groups (Table 2).

Histopathological examination of isolated rat liver tissues revealed steatosis in the form of fat deposition in hepatocytes in group IIA, and steatohepatitis in the form of fat deposition in hepatocytes surrounded by aggregates of chronic inflammatory cells indicating inflammation in group IIB (Fig. 1).
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Table (1): Comparison of all measured parameters in all studied groups (Mean ± SD).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Group IA</th>
<th>Group IIA</th>
<th>Group IB</th>
<th>Group IIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final BW (g)</td>
<td></td>
<td>226.27±8.09</td>
<td>319.68±8.62</td>
<td>246.07±10.16</td>
<td>409.81±10.10</td>
</tr>
<tr>
<td>Final BMI (gm/cm²)</td>
<td></td>
<td>0.54±0.03</td>
<td>0.76±0.06</td>
<td>0.56±0.04</td>
<td>0.94±0.07</td>
</tr>
<tr>
<td>Final AC (cm)</td>
<td></td>
<td>15.18±0.71</td>
<td>18.21±0.98</td>
<td>15.73±0.71</td>
<td>21.41±0.78</td>
</tr>
<tr>
<td>Nesfatin-1 (ng/ml)</td>
<td></td>
<td>3.13±0.46</td>
<td>4.01±0.63</td>
<td>3.03±0.35</td>
<td>5.54±0.49</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td></td>
<td>84.45±5.70</td>
<td>146.05±5.60</td>
<td>86.47±5.15</td>
<td>218.63±9.41</td>
</tr>
<tr>
<td>Insulin (µIU/ml)</td>
<td></td>
<td>20.02±1.45</td>
<td>31.33±3.00</td>
<td>20.03±1.23</td>
<td>41.01±2.14</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td></td>
<td>4.18±0.39</td>
<td>11.29±1.12</td>
<td>4.28±0.39</td>
<td>22.13±1.45</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td></td>
<td>74.94±5.29</td>
<td>127.22±7.93</td>
<td>76.94±5.63</td>
<td>164.10±5.92</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td></td>
<td>43.49±5.23</td>
<td>77.30±7.91</td>
<td>47.53±3.92</td>
<td>108.72±8.55</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td></td>
<td>43.12±3.06</td>
<td>34.10±3.54</td>
<td>43.13±2.95</td>
<td>26.05±2.39</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td></td>
<td>23.12±4.87</td>
<td>77.66±8.26</td>
<td>24.31±7.42</td>
<td>115.71±6.78</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td></td>
<td>8.70±1.05</td>
<td>15.46±1.58</td>
<td>9.51±0.78</td>
<td>21.74±1.71</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td></td>
<td>39.37±3.70</td>
<td>86.90±7.07</td>
<td>40.33±4.66</td>
<td>130.19±6.39</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td></td>
<td>145.48±7.37</td>
<td>161.09±6.33</td>
<td>142.96±4.52</td>
<td>184.13±7.72</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td></td>
<td>0.034±0.01</td>
<td>0.084±0.01</td>
<td>0.038±0.01</td>
<td>0.116±0.01</td>
</tr>
</tbody>
</table>

(*): significant versus group IA, (**): significant versus group IIA, (***): significant versus group IB.

Table (2): Correlation of serum levels of nesfatin-1 with the measured parameters in all studied groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Group IA</th>
<th>Group IIA</th>
<th>Group IB</th>
<th>Group IIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final BW (g)</td>
<td></td>
<td>0.506</td>
<td>0.790**</td>
<td>0.238</td>
<td>0.942***</td>
</tr>
<tr>
<td>Final BMI (gm/cm²)</td>
<td></td>
<td>0.060</td>
<td>0.817**</td>
<td>0.116</td>
<td>0.789**</td>
</tr>
<tr>
<td>Final AC (cm)</td>
<td></td>
<td>0.132</td>
<td>0.838**</td>
<td>0.067</td>
<td>0.687</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td></td>
<td>0.440</td>
<td>0.675*</td>
<td>0.135</td>
<td>0.927***</td>
</tr>
<tr>
<td>Insulin (µIU/ml)</td>
<td></td>
<td>0.316</td>
<td>0.644*</td>
<td>0.322</td>
<td>0.936***</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td></td>
<td>0.179</td>
<td>0.739**</td>
<td>0.029</td>
<td>0.849**</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td></td>
<td>0.106</td>
<td>0.754**</td>
<td>0.394</td>
<td>0.781**</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td></td>
<td>0.167</td>
<td>0.696*</td>
<td>0.238</td>
<td>0.665</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td></td>
<td>-0.407</td>
<td>-0.704*</td>
<td>-0.104</td>
<td>-0.917***</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td></td>
<td>0.188</td>
<td>0.897***</td>
<td>0.368</td>
<td>0.823**</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td></td>
<td>0.414</td>
<td>0.735**</td>
<td>0.239</td>
<td>0.821**</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td></td>
<td>0.203</td>
<td>0.820**</td>
<td>0.522</td>
<td>0.834**</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td></td>
<td>0.079</td>
<td>0.811**</td>
<td>0.428</td>
<td>0.784**</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td></td>
<td>0.463</td>
<td>0.700*</td>
<td>0.238</td>
<td>0.832**</td>
</tr>
</tbody>
</table>

(r): correlation versus nesfatin-1, (\(\ast\)): significant (P<0.05), (\(\ast\)\(\ast\)): significant (P<0.01), (\(\ast\)\(\ast\)\(\ast\)): significant (P<0.001).
Figure (1): Photomicrographs of isolated rat liver tissues stained with Hematoxylin and Eosin: (A): Normal liver tissues formed of normal-sized central vein (*) surrounded by rows and cords of normal hepatocytes with central nuclei and abundant eosinophilic cytoplasm in group IA. (B): Marked fatty change of hepatocytes (↑) with central nuclei and clear cytoplasm in group IIA indicating steatosis. (C): Normal liver tissue with normal-sized central vein (*) surrounded by normal hepatocytes with central nuclei and abundant eosinophilic cytoplasm in groups IB. (D): Hepatocytes with fat infiltration and clear cytoplasm surrounded by aggregates of chronic inflammatory cells (†) in group IIB. (x 400).

DISCUSSION

In the present study, the induction of obesity model in rats using HFD for 4 and 12-week duration was confirmed by the significant progressive rise in the final body weight, BMI, HOMA-IR index and serum levels of glucose, insulin and lipid profile parameters except HDL that significantly decreased in HFD groups compared with control groups. These findings involved many signs of the metabolic syndrome specially insulin resistance (IR), type II diabetes mellitus (DM) and dyslipidemia (Han and Lean, 2016) and are consistent with those of other studies (Eisinger et al., 2014 and Yu et al., 2014).
In addition, the successful induction of NAFLD rat model in the present study was established by the histopathological examination of isolated liver tissues that revealed fatty infiltration in group IIA indicating simple steatosis and chronic inflammatory cell infiltration in group IIB indicating steatohepatitis. These findings were accompanied by a significant time-dependant increase in serum levels of ALT and AST in HFD groups. Consistent with our findings, several studies reported the successful induction of hepatic steatosis and steatohepatitis in rats using HFD (Freitas et al., 2016 and Wu et al., 2016).

The occurrence of hepatic steatosis in our study can be explained by the down regulating effect of HFD on hepatic LDL receptors which resulted in decreased hepatic LDL clearance, prolongation of plasma half-life of VLDL and LDL and consequently steatosis (Bieghs et al., 2012). Another explanation may be through the occurrence of IR which was established in the present study based on finding a significant rise in glucose and insulin serum levels and HOMA-IR index. Peripheral IR was reported to induce hepatic steatosis through decreasing the suppressing effect of insulin on glucose production in the liver which cause deterioration of peripheral IR and initiate lipogenesis in the liver (Gastaldelli et al., 2007). Moreover, IR was found to inhibit β-oxidation of free fatty acids leading to accumulation of hepatic lipids (Postic and Girard, 2008). Furthermore, the anti-lipolytic action of insulin in adipose tissue was reported to be impaired by IR leading to an increased release of free fatty acids, which disturbs lipid metabolism and consequently may induce steatosis (Gaggini et al., 2013). The increase of plasma free fatty acids levels as a consequence of obesity or HFD-feeding was found to induce IR and low-grade inflammation (Mantzaris et al., 2011). Additionally, the in-vivo studies showed that saturated fatty acids participate in generation of IR, hepatic steatosis and activation of pro-inflammatory M1 macrophages through activation of the c-Jun terminal kinase (JNK) (Gadang et al., 2013). Other in-vivo studies demonstrated that palmitate triggered oxidative stress in hepatocytes endoplasmatic reticulum (Leamy et al., 2014) and activated macrophages inducing inflammation (Snodgrass et al., 2013). Also, ceramides, which are synthesized from long-chain saturated fatty acids in the endoplasmatic reticulum of hepatocytes, were reported to be involved in hepatic insulin resistance and to have lipotoxic effect on pancreatic cells (Ussher et al., 2010). Furthermore, it was demonstrated that insulin triggers de novo lipogenesis and glyceroneogenesis pathways (Saponaro et al., 2015) which were found to be increased in NAFLD contributing to the development of hepatic steatosis (Hyotylainen et al., 2016).

Compared with control groups, the present study demonstrated a significant rise in serum nesfatin-1 levels in HFD groups that increased with the increase in the duration of HFD in male albino rats. Additionally, positive significant correlations were found between serum levels of nesfatin-1 and all measured parameters with the exception of HDL which showed negative correlation in both HFD groups. In agreement with our results, the study by Wu et al. (2016) demonstrated increased plasma nesfatin-1 levels in NAFLD model induced by HFD.
for 4 weeks in rats. On the contrary to our findings, it was reported that serum levels of nesfatin-1 in patients with NAFLD significantly reduced in comparison to healthy controls, significantly reduced in obese subjects compared with non-obese subjects, and significantly reduced in insulin-resistant subjects compared with insulin-sensitive ones (Basar et al., 2012).

The present study could not determine the precise reason underlying the increased nesfatin-1 levels in NAFLD rat model. Nesfatin-1 was considered as anorexigenic factor that regulates food intake and gastrointestinal functions (Stengel & Taché, 2011 and Stengel et al., 2011). Stengel et al. (2009) reported the increase in circulating and gastric nesfatin-1 after reducing food intake. Another study revealed that food intake was restricted when nesfatin-1 was injected intraperitoneally (Shimizu et al., 2009). Moreover, Atsuchi et al. (2010) reported that central nesfatin-1 administration reduced food intake. Also, the study by García-Galiano et al. (2010) demonstrated that intracerebroventricular injection of nesfatin-1 caused dose-dependent decrease in food intake in adult rats and the long-standing administration of nesfatin-1 led to decrease in body weight. Therefore, the primary stimulus for the increase in nesfatin-1 levels in our study may be feeding the rats with high-fat diet.

Our results revealed that nesfatin-1 correlated positively with BMI (Tsuchiya et al., 2010 and Basar et al., 2012).

The current study found that nesfatin-1 correlated positively with glucose, insulin and HOMA-IR index in both HFD groups. Consistent with our findings, Zhang et al. (2012) reported the increase in plasma levels of nesfatin-1 in patients with type II DM. Additionally, the studies by Foo et al. (2010) and Gonzalez et al. (2011a) revealed the expression of nesfatin-1 in rat islet beta cells of pancreas and reported the stimulation of its secretion by high glucose in vitro. Furthermore, it was found that nesfatin-1 improved insulin secretion stimulated by glucose in mouse and rat pancreatic β cells (Gonzalez et al., 2011b; Nakata et al., 2011 and Gonzalez et al., 2012). Moreover, Li et al. (2012) found that basal nesfatin-1 levels significantly increased by intravenous infusion of glucose in healthy adults. Therefore, the present study suggested that hyperglycemia may be another explanation for the increased nesfatin-1 levels in rat model of NAFLD induced by HFD. In contrast to the previous reports, another study reported that nesfatin-1 correlated negatively with fasting blood glucose and insulin resistance (Basar et al., 2012).

Our results revealed that nesfatin-1 levels correlated positively with liver enzymes (ALT and AST) and the inflammatory marker (CRP) in both HFD groups. This finding was consistent with the results of other studies (Saldanha et al., 2012 and Zhang et al., 2012). In contrast, other studies found that nesfatin-1 correlated negatively with BMI (Tsuchiya et al., 2010 and Basar et al., 2012).
tion for the disturbed glucose and lipid metabolism in rat model of NAFLD. This hypothesis was supported by the study of Su et al. (2009) which demonstrated that administration of nesfatin-1 to hyperglycemic rats produced anti-hyperglycemic effect that was attributed to its inhibitory effect on hepatic production of glucose by modulating glycogen synthesis and gluconeogenesis. Additionally, it was found that nesfatin-1 inhibited glucose production in the liver when injected centrally by diminishing the production of the phosphoenolpyruvate carboxykinase enzyme (Yang et al., 2012).

The present study also, suggested that the increased nesfatin-1 levels in NAFLD rat model might be a compensation for the inflammation present in steatohepatitis through its anti-apoptotic and anti-inflammatory properties. Consistent with this suggestion, it was reported that nesfatin-1 inhibited neutrophil infiltration and inflammatory responses that depend on nuclear factor kappa-B and reducing neuronal cell apoptosis mediated by caspase-3 after traumatic brain injury in rats (O’zsavci et al., 2011 and Tang et al., 2012).

CONCLUSION

The present study revealed that feeding rats with HFD for 4 and 12 consecutive weeks could successfully induce steatosis and steatohepatitis, respectively in rats that was indicated by obesity, disturbed glucose and lipid metabolism and liver dysfunction. Also, our results demonstrated a progressive time-dependent increase in serum levels of nesfatin-1 that correlated positively with the anthropometric parameters, glycemic control parameters, liver enzymes, CRP and lipid profile parameters, apart from HDL that correlated negatively with nesfatin-1 in both HFD groups. The increase in serum nesfatin-1 levels might be attributed to feeding rats with HFD or hyperglycemia or may be a compensatory mechanism to improve the metabolic and liver dysfunction through its anorexigenic, anti-hyperglycemic and anti-inflammatory effects. Further studies are required to elucidate nesfatin-1 role in the pathogenesis of NAFLD and to explore the potential therapeutic role of nesfatin-1 in NAFLD.

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REFERENCES


BACKGROUND: Nesfatin-1 is a peptide hormone that regulates energy homeostasis by controlling food intake and glucose homeostasis in the blood. It is also involved in the regulation of the liver and has been implicated in the pathogenesis of alcoholic liver disease. However, the role of nesfatin-1 in non-alcoholic fatty liver disease (NAFLD) remains unclear. The study aimed to investigate the levels of nesfatin-1 in male rat models with NAFLD.

MATERIALS AND METHODS: Male rats were divided into two groups: (IA and IB) receiving a standard diet for 4 weeks followed by 12 weeks of a high-fat diet, and (IIA and IIB) receiving a high-fat diet for the same period. The study measured body weight and composition, nesfatin-1 levels, insulin, and glucose levels, as well as inflammatory markers and hepatic enzymes.

RESULTS: The study showed that nesfatin-1 levels increased significantly in both groups with high-fat diet compared to standard diet. There was also a significant increase in insulin and glucose levels, and a decrease in hepatic enzymes.

CONCLUSION: The study suggests that nesfatin-1 may play a role in the pathogenesis of NAFLD, possibly through its effects on energy homeostasis and liver function.
الدهون باستثناء البروتينات الدهنية عالية الكثافة والتي أظهرت إنخفاضًا ذا دلالة إحصائية في مصل دم الجرذان في المجموعتين التي تم تغذيتها بغذاء عالي الدهن بالمقارنة بالمجموعة الضابطتين. علاوة على ذلك، فقد كان هناك ارتباط إيجابي ذا دلالة إحصائية بين مستويات النسفانتين-1 وجميع القياسات السابقة في المجموعتين التي تم تغذيتها بغذاء عالي الدهن باستثناء البروتينات الدهنية عالية الكثافة حيث ارتبطت ارتباطًا عكسيًا ذا دلالة إحصائية بالنسفانتين-1.

الاستنتاج: نستخلص من هذه الدراسة أن هناك زيادة في مستويات النسفانتين-1 في مصل دم الجرذان المحدث بهما تجريبياً نموذج مرض الكبد الدهني الغير كحولي وهذه الزيادة ربما تعزى إلى تغذية الجرذان بالغذاء عالي الدهن، أو ربما إلى زيادة مستوى الجلوكوز في الدم، أو من الممكن أن تكون لتعويض الالتهاب والتمثيل الغذائي المضطرب.