



Original article

Variation and significance of serum leptin, blood lipid level, adiponectin, NO and TNF- α for patients with non-traumatic ischemic necrosis of the femoral head

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ABSTRACT

Objective: To investigate the changes of serum leptin, lipid levels, adiponectin, NO and TNF- α in patients with non-traumatic ischemic necrosis of the femoral head of the femoral head and its meanings.

Methods: A total of 80 patients with ischemic necrosis of the femoral head were selected from January 2015 to January 2016. And 30 healthy volunteers who took the same time were selected as the control group. Both subjects were given venous blood in the morning fasting. Serum leptin levels were measured by radioimmunoassay. Serum lipids, high and low density lipoprotein, cholesterol, triglyceride and apolipoprotein A1 were detected by automatic biochemical analyzer. Apolipoprotein B was measured by radioimmunoassay. The levels of serum adiponectin were measured by radioimmunoassay. The levels of NO and TNF- α in serum were measured by enzyme-linked immunosorbent assay (ELISA).

Results: Compared with the control group, the levels of cholesterol, triglyceride level, middle and low density lipoprotein and apolipoprotein B were significantly increased in INFH serum; the levels of high density lipoprotein and apolipoprotein A1 were significantly decreased. The contents of NO and TNF- α were significantly increased, the content of adiponectin was significantly decreased. There was significant difference between the two groups ($P < .05$).

Conclusion: The levels of serum cholesterol, triglyceride level, low density lipoprotein level, apolipoprotein B level, leptin, NO and TNF- α levels in serum of INHF patients were positively correlated with the condition of INHF patients, and high density lipoprotein levels, Apolipoprotein A1 levels and adiponectin levels were negatively correlated with INHF patients.

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1. Introduction

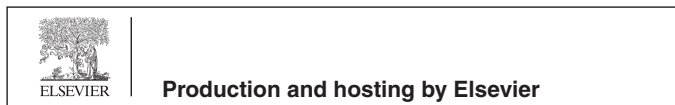
Ischemic necrosis of the femoral head (ischemic necrosis of the femoral head, INFH) is a common disease in clinical practice, and it usually occurs in young adults; lesion occurs at the lesion site, which may be accumulated at the whole hip joint, finally resulting in function loss of hip joint and seriously affecting the patients' health and life quality (Liu et al., 2017; Zhu and Zhu, 2012). The

pathogenesis inducing INFH is complex, blood supply insufficiency of femoral head is a key factor resulting in INFH, it is reported according to many reports that hyperlipidemia is closely related to INFN (Zhang et al., 2012), while leptin plays an important role in many linkages of human metabolic process (Liu et al., 2012); as a kind of endogenous bioactive polypeptide of adipose tissue secretion, adiponectin is able to reflect human lipid metabolism level to a certain degree (Huang, 2015); it is also reported that the level of NO, TNF- α and other correlation factors of INHF patients has relevance with the bone marrow edema of INFH and pain degree (Lin et al., 2012). Therefore, 80 patients with non-traumatic ischemic necrosis of the femoral head admitted in orthopedics department of our hospital from January 2015 to January 2016 were selected as the object of the study, studying the variation of serum leptin, blood lipid level, adiponectin, NO and TNF- α of patients with non-traumatic ischemic necrosis of the femoral

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head to provide with theoretical basis for the further study on molecular mechanism, and the reports are as follows.

2. Information and method

2.1. General Information

80 patients with non-traumatic ischemic necrosis of the femoral head admitted in orthopedics department of our hospital from January 2015 to January 2016 were selected as the object of the study, and refer to the staging standard of ARCO (The association research circulation osseous, ARCO) for the diagnostic criteria. 59 males, 21 females, aged from 32 to 61, and the average age (45.27 ± 7.41); the body mass index (BMI) $20.45\text{--}27.64 \text{ m}^2/\text{kg}$, and the average BMI is (24.67 ± 4.85) m^2/kg ; grouping is conducted according to pathogenesis, 26 for hormone type, 38 for alcohol type and 16 for special type. 30 healthy volunteers taking physical exam in our hospital at the same period were selected as control group, in which males are 20, females are ten, aged from 33 to 63 years old and the average age is (46.38 ± 6.37); the body mass index (BMI) is $21.67\text{--}28.27 \text{ m}^2/\text{kg}$, and the average value is (25.34 ± 5.07) m^2/kg . There is no statistical difference ($P > .05$) between the healthy volunteers and INFH patients in age, gender, body mass index and other comparisons, and there is comparability. All patients signed on the informed consent under the approval of ethics committee of our hospital.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) according to the staging of femoral head necrosis based on ARCO, the morbidity extent of all patients is at stage I and II; (2) patients are aged from 18 to 70 years old; (3) diagnosed as non-traumatic ischemic femoral head necrosis; (4) usually work on mild and medium jobs.

Exclusion criteria: (1) patients with severe osteoporosis; (2) patients combined with other systemic immune diseases; (3) patients combined with hypertension, heart diseases and other internal diseases; (4) patients with mental diseases.

2.3. Observational index

4 ml venous blood was taken from both INFH patients and healthy volunteers when they were empty stomach in the morning. Then, the blood is centrifuged at 35 rpm for 15 min and the serum is obtained and stored at -80°C . (1) Radioimmunoassay was adopted for serum leptin level determination of subjects in both groups, and the kit was purchased from Beijing Huabu Biological Technology Research Institute; (2) automatic biochemical analyzer was adopted for determining high-density lipoprotein, lipoprotein at medium and low density, cholesterol, triglyceride, apolipoprotein A1 and apolipoprotein B level in serum of subjects for both groups; (3) radioimmunoassay was adopted for determining the level of adiponectin in the serum of subjects for both groups, and the kit is purchased from Beijing Huabu Biological Technology Research Institute; (4) enzyme linked immunosorbent assay (ELISA) was adopted for determining NO and TNF- α level in the serum of subjects for both groups. All of the above operations are strictly subject to the respective kit introductions to guarantee the objectivity of the results.

2.4. Statistical method

SPSS 17.0 statistical analysis software was adopted for processing and researching on all data, the method of double entry check was adopted for all data, the form of ($\bar{x} \pm s$) was adopted for mea-

surement data, and *t* is applied to inspection; the form of (*n*, %) was adopted for enumeration data, and chi-square (χ^2) is applied to inspection; when $P < .05$, the difference has statistical significance.

3. Results

3.1. Comparison of blood lipid level in serum between the subjects of two groups

Determination on blood lipid level of subjects in both groups were conducted, cholesterol level, triglyceride level, lipoprotein level at medium and low density and apolipoprotein B level of INFH patients were significantly higher than those of the control group, high-density lipoprotein level and apolipoprotein A1 level were significantly lower than those of the control group, and there was statistical difference ($P < .05$) between the difference of both groups, see Table 1.

3.2. Comparison of leptin and adiponectin level in the serum of subjects for both groups

Compared with the control group, the leptin level in the serum for INHF patients (both male and female) in the serum was significantly increased, adiponectin level was obviously lowered, and there was statistical difference between the difference of both groups ($P < .05$), see Table 2.

3.3. Comparison of NO and TNF- α level in the serum of subjects for both groups

Compared with the control group, the NO and TNF- α level in the serum of INHF patients were significantly increase, and there was statistical difference ($P < .05$) between the difference of both groups, see Table 3.

4. Discussion

INHF is a common disease in clinical practice, mainly because the blood supply of femoral head is damaged, resulting in ischemia of femoral head, cell death and finally femoral head necrosis. At the later period of INHF, it results in bone collapse and osteoarthritis, seriously affecting the health and life quality of the patients. Its pathogenic factors are complex, and the pathogenic factor determined includes chronic alcohol drinking, hormone injection, etc. (Wang et al., 2017). Therefore, researching on pathogenesis of INHF and molecular level variation of INHF patients is able to provide with theoretical basis for the treatment and prevention of INHF.

INHF patients are often accompanied with lipid level rise and lipid peroxidase accumulation, chronic alcoholism results in hyperlipidemia and fatty liver and reduces the metabolic capability of hepatic cell to lipid, causing the rise of cholesterol and triglyceride level in the blood; when the intravascular lipid is accumulated to a certain degree, it results in endovascular stenosis and intraosseous pressure rise, affecting arterial perfusion and venous return and excretion of metabolites, further aggravating the obstruction of blood vessels (Ma and Ai, 2012). This kind of vicious circle continues, which finally results in obstruction of femoral head blood vessel, forming into INHF. The long-term and a lot of hormone injection reduces the activity of osteocyte and facilitates the secretion of adrenal cortex hormone; the cortisol secretion increases and accumulated in the blood, which inhibits the activity of osteocyte and reduces the synthesis of protein, mucopolysaccharide and others, inhibiting synthesis of osteoblasts, reducing the number of osteoblasts, resulting in osteoporosis and aggravating the degree of fracture (Feng and Sun, 2016; Li et al., 2013). There-

Table 1Comparison of blood lipid level in the serum of subjects for both groups [$\bar{x} \pm s$].

Groups	Cholesterol (nmol/L)	Triglyceride (nmol/L)	High-density lipoprotein (mmol/L)	Lipoprotein at medium and low density (mmol/L)	Apolipoprotein A1 (g/L)	Apolipoprotein B (g/L)
Control group (n = 30)	3.87 ± 0.84	1.03 ± 0.51	1.52 ± 0.64	2.16 ± 0.97	1.52 ± 0.53	0.75 ± 0.30
INHF group (n = 80)	4.72 ± 1.24	1.67 ± 0.85	1.08 ± 0.53	2.84 ± 1.20	1.09 ± 0.34	0.98 ± 0.38
t	4.112	4.810	3.659	2.779	4.136	2.982
P value	0.001	0.000	0.001	0.006	0.000	0.004

Table 2Comparison of leptin and adiponectin level in the serum of subject for both groups [$\bar{x} \pm s$].

Groups	Leptin (μg/L)		Adiponectin (μg/mL)	
	Male	Female	Male	Female
Control group	5.27 ± 1.37	12.87 ± 7.46	17.64 ± 7.65	21.74 ± 8.24
INHF group	18.42 ± 6.74	25.41 ± 10.57	6.87 ± 2.47	8.62 ± 3.41
t	14.149	3.361	6.188	4.842
P value	0.000	0.002	0.000	0.001

Table 3Comparison of NO and TNF-α level in the serum of subjects for both groups [$\bar{x} \pm s$].

Groups	NO (μmol/L)	TNF-α (μg/L)
Control group (n = 30)	6.27 ± 0.94	1.87 ± 0.37
INHF group (n = 80)	23.74 ± 8.69	16.77 ± 6.42
t	17.707	20.667
P value	0.000	0.000

fore, the study researched the variation of serum leptin, blood lipid level, adiponectin, NO and TNF-α in INHF patients and explored the significance of its variation.

Leptin combines with leptin binding protein in the body, participates in various physiological processes of the body, it can facilitate the decomposition of triglyceride, inhibit the synthesis of fatty acid synthetase and fat synthesis and promote the fat metabolism. And it is indicated through researches that leptin is able to mediate the balanced relation between fat amount and bone mass, and the leptin content of female patients is 2–3 times of males (Wang et al., 2012; Wang, 2013). It is indicated through researches that the leptin level in INHF patients is significantly increased, and it can adjust the bone metabolism through direct action on osteoblasts. The blood lipid metabolism in INHF patients is seriously in disorder, while vascular thrombosis caused by hyperlipidemia is one of important causes inducing INHF (Lu et al., 2016); it is reported that the blood viscosity of INHF patients is increased, the blood lipid level is increased and the hemodynamics is abnormal. Apolipoprotein A1 plays the role of cholesterol removal in the body, while apolipoprotein B mainly exists in the surface of low-density lipoprotein, playing the role of identification, and its content increase may increase the occurrence of coronary heart disease, hyperlipidemia and other diseases. According to the research, it is showed that cholesterol level, triglyceride level, lipoprotein level at medium and low density and apolipoprotein B level of INHF patients are significantly increased, high-density lipoprotein level and apolipoprotein A1 level are significantly lowered, and the leptin content in the serum is significantly increased, similar to the results of the previous researches; it is showed that INHF patients are usually accompanied with the occurrence of hyperlipidemia, and the variation of substances in the body related to lipid metabolism is obvious, which should be treated actively to reduce the accumulation of blood lipid. Real-time monitoring should be conducted on patients with higher blood lipid content to prevent the occurrence of INHF.

It is reported that adiponectin is a kind of independent factor that may predict INHF, and it is related to height, weight, age, blood lipid level and other factors (Fu and Zheng, 2015). As an insulin hypersensitizing hormone, adiponectin may increase and facilitate the fatty acid oxidation and glucose absorption of skeletal muscle cell, which is positively related to triglyceride and low-density lipoprotein and negatively related to high-density lipoprotein. Lowering of adiponectin content indicates the occurrence of hyperlipidemia atherosclerosis. What's more, it can reduce the expression of adherence factor in endothelial cell, inhibiting the activation of NF-κB path, inhibiting the generation of TNF-α and other inflammatory factors and playing a certain anti-inflammatory effect (Ma et al., 2016). Osteoarthritis is an important manifestation of INHF later period; as an important inflammatory factor, TNF-α is positively related to the morbidity extent of osteoarthritis. It cannot only facilitate the generation of collagenase and PEG₂, facilitate the decomposition of the bone and increase the toxic effect on osteocyte, but can also aggravate the permeability of endothelial cells and edema (Lu et al., 2004). NO plays important roles in the body, such as facilitate angiectasis, cytotoxicity, neural signaling and other effects. It is reported that NO and TNF-α level in the serum of INHF patients are positively related to the morbidity extent of INHF. It is showed according to the research results that adiponectin content in the serum of INHF patients is significantly reduced, and the content of NO and TNF-α is significantly increased, similar to the results of the previous researches.

In conclusion, cholesterol level, triglyceride level, lipoprotein level at medium and low density, apolipoprotein B level, leptin, NO and TNF-α level in serum of INHF patients are positively correlated to the condition of INHF patients, while lipoprotein level at high density, apolipoprotein A1 level and adiponectin level are negatively related to the condition of INHF patients.

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