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Original article

Effect of lipid lowering tablet on blood lipid in hyperlipidemia model rats

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ABSTRACT

Observe the effect of lipid-lowering tablets on body weight, liver index and serum biochemical indexes of hyperlipidemia rats. The hyperlipidemia rat model was replicated successfully. Compared with the model group, high, medium and low dose lipid-lowering tablets group could significantly increase the body weight of rats with hyperlipidemia ($P < 0.01$, $P < 0.05$); High and middle dose lipid-lowering tablets group could significantly reduce the liver index of high fat rat ($P < 0.01$); High, medium and low dose lipid-lowering tablets group could significantly decrease levels of TC, TG, LDL-C, AST, ALT, ALP, Y-GT in serum ($P < 0.01$, $P < 0.05$), and significantly increase the level of HDL-C ($P < 0.01$). Lipid-lowering tablets can effectively regulate the body lipid metabolism of rats, and have a certain therapeutic effect on hyperlipidemia.

1. Introduction

With the rapid development of social productivity and social economy, people's living standard has been improved to some extent. The gradual intake of high-sugar, high-fat and high-protein foods has changed people's dietary structure, so that the body lipid metabolism disordered, antioxidant capacity reduced, lipid oxidation products increased, resulting in atherosclerotic vascular injury (Ye et al., 2014). Hyperlipidemia can lead to atherosclerosis, and then lead to coronary heart disease, stroke, diabetes complications, myocardial infarction and other diseases, and many other diseases of other systems of the body are also closely related to it, being the first killer of human health. By 2030, cardiovascular disease will still be the leading cause of death in humans, and nearly 23 million 600 thousand people will die from cardiovascular disease (Wang et al., 2013; Gao et al., 2017). As a traditional feature of our country, the traditional Chinese medicine has its unique effect and obvious advantages in prevention and treatment of hyperlipidemia, and is also one of the ways for the treatment of hyperlipidemia (Gohar et al., 2017). We should take comprehensive measures to give full play to the advantages of combining traditional Chinese and Western medicine, to prevent and reduce the risk factors of atherosclerosis, and this is also an important aspect of cardiovascular disease research in China (Ge et al., 2016; He et al., 2016). This model of hyperlipidemia was established by compound factor modeling of high fat diet and fat emulsion, to observe the intervention effect of lipid-lowering tablets on body weight, liver index and serum biochemical indexes of hyperlipidemia rats.

1.1. Animals

Rat, Species: Wistar, Grade: SPF, male, 180–220 g, Certificate Number: 37009200001785, Provide Unit: Shandong Lukang Pharmaceutical Co. Ltd. License No. SCXK (Lu) 2014005.

1.2. Experimental drugs and reagents

Lipid-lowering tablets, preparation room of the 371st Central Hospital of PLA in Xinxiang, batch number 20150806; Xuezhikang Capsule, Beijing Beida Weixin biotechnology Co. Ltd., batch number: 20150718; Propylene glycol, Tianjin Zhiyuan Chemical Reagent Co. Ltd., batch number: 20150320; Twain -80, Tianjin Fu Yu Fine Chemical Co. Ltd., batch number: 20150410.

Sodium deoxycholate, Beijing Aoboxing biotechnology limited liability company, batch number: 20160112; Propylthiouracil

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Tablets, Shanghai Zhaohui Pharmaceutical Co. Ltd., batch number: 1506N18; Cholesterol, Zhengzhou Paini chemical reagent factory, batch number: 20151220; Saline, Beverly Henan Shuanghe Pharmaceutical Co. Ltd., batch number: 20160108; T-CHO test kit, batch number: A111-1; TG test kit, batch number: A1101-1; HDL-C test kit, batch number: A112-1; LDL-C test kit, batch number: A113-1; AST test kit, batch number: C010-1; ALT test kit, batch number: C009-2; Y-GT test kit, batch number: C017. The test kit was purchased Nanjing Jiancheng Institute of biological engineering.

High fat emulsion configuration: oil phase: lard 25 g, cholesterol 10 g, propylthiouracil tablets 1 g, polysorbate 80 25 ml; aqueous phase: distilled water 30 ml, propylene glycol 20 ml, sodium deoxycholate 2 g. Preparation method: oil phase: add lard 25 g into a 200 ml beaker, heat to 100 °C, add cholesterol 10 g to melt, add propylthiouracil tablets 1 g, and after a fully mix, add polysorbate 80 25 ml; aqueous phase: add distilled water 30 ml to a 200 ml beaker, bath with 60 °C water bath, add propylene glycol 20 ml, sodium deoxycholate 2 g to fully dissolve; then add aqueous phase into the oil phase, stir, and cool down in the 4 °C refrigerator for further use (Muhammad et al., 2017a).

High fat diet configuration: 10% lard, 1% cholesterol, 5% egg yolk powder, 0.2% propylthiouracil, 0.5% sodium deoxych sodium deoxycholate, 5% sucrose, 78.3% basic feed for proportion.

2. Experimental instrument

FA (N)/JA (N) series electronic balance, Shanghai Mingqiao Precision Instrument Co. Ltd.; HWS12 type electric thermostatic water bath, Shanghai Hengyi Scientific Instrument Co. Ltd.; KDC-160HR high-speed refrigerated centrifuge, Zhongjia branch of Keda Innovation Co. Ltd. by Share; type 680 microplate reader, US BIO-RAD Company.

2.1. Statistics method

Analyze data using SPSS17.0 statistical package for medical data, express measurement data as average ± standard deviation ($(\bar{x} \pm s)$), use Ridit test for rank data.

2.2. Methodology

72 male rats were randomly divided into 6 groups after 3-day adaptive feeding in the lab, with 12 rats in each group, respectively as control group, model group, Xuezhikang group, high, medium and low dose lipid-lowering tablets group (Li et al., 2016). Except for the blank control group, the other groups were fed with high fat diet and were given fat emulsion by gavage, to establish the model of hyperlipidemia by compound factor modeling (Wang et al., 2014; Peng et al., 2013). At the same time, the blank control group and the model group were given the same volume of saline by gavage. In every morning gavage every rat in drug groups with corresponding drugs, and in the afternoon gavage each rat with fat emulsion (Chen et al., 2014). For Xuezhikang group (0.2 g/kg), high, medium and low dose lipid-lowering tablets group (1.5 g/kg, 0.75 g/kg, 0.375 g/kg). Gavage rats with the dose standard of 1 ml/100 g. In the afternoon, gavage all other groups except the control group with high fat emulsion (Muhammad et al., 2017b). Corresponding drugs were given by gavage for 21 days. After 2 h of administration at the 21st day, removed eyeball, collected blood, after the stratification at room temperature, put into the centrifuge and run at 3000 r/min for 10 min, separated the serum, stored separately in -20 degrees for cryopreservation and collected data of biochemical indexes, including total cholesterol, triglyceride, high density lipoprotein cholesterol, low density lipoprotein cholesterol, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase (Guo et al., 2011). Rats were sacrificed by the method of neck dissection, liver was removed and weighed, and the relative weight of the liver was calculated (liver index = liver weight/body weight $*$ 100%).

3. Results

As can be seen from Table 1, for the first time, there was no difference among groups, meaning that grouping was uniform (Yu and Gao, 2016). Compared with the control group, rats in the model group had significantly slower weight growth in one week, two weeks, and three weeks, having significant differences in body weight with the blank control group ($P < 0.01$), which showed that the model of hyperlipidemia was successful. Compared with the model group, in the first week, high, medium and low dose lipid-lowering tablets group and Xuezhikang group could significantly increase the body weight of hyperlipidemia rat ($P < 0.01$); In second weeks, high dose lipid-lowering tablets group and Xuezhikang group could significantly increase the body weight of hyperlipidemia rats ($P < 0.01$), medium lipid-lowering tablets group could significantly increase the body weight of hyperlipidemia rats ($P < 0.05$); In third weeks, the high and middle dose lipid-lowering tablets group and Xuezhikang group could significantly increase the body weight of hyperlipidemia rats ($P < 0.01$).

As can be seen from Table 2, compared with the blank control group, the liver index of model group significantly increased

Table 2
Effect of lipid lowering tablet on liver index of hyperlipidemia model rats.

Group	n	Liver index (mg/g)
Control group	12	28.33 ± 2.36**
Model group	12	33.80 ± 1.64
Xuezhikang group	12	29.37 ± 2.20**
High dose group	12	30.38 ± 1.73**
Middle dose group	12	30.59 ± 1.86**
Low dose group	12	31.33 ± 3.28

Notes: Compared with model group.
* $p < 0.05$.
** $p < 0.01$.

Table 1
Effect of lipid lowering tablet on body weight of hyperlipidemia model rats (N = 12).

Group	First time	One week	Two weeks	Three weeks
Control group	211.53 ± 7.62	280.68 ± 13.12**	312.68 ± 13.69**	347.43 ± 17.97**
Model group	209.26 ± 6.48	249.90 ± 9.75	258.18 ± 14.02	256.79 ± 16.87
Xuezhikang group	210.00 ± 9.49	264.02 ± 10.38**	271.38 ± 12.87**	274.98 ± 15.13**
High dose group	207.68 ± 5.02	270.36 ± 10.73**	274.42 ± 11.11**	276.08 ± 9.92**
Middle dose group	208.73 ± 6.41	273.55 ± 14.70**	270.58 ± 9.63*	272.72 ± 10.72**
Low dose group	210.61 ± 6.12	269.44 ± 9.99**	266.27 ± 9.92	259.00 ± 10.47

Notes: Compared with model group.
* $p < 0.05$.
** $p < 0.01$.

Table 3
Effect of lipid lowering tablet on serum biochemical index of hyperlipidemia model rats (N = 12).

Group	TG (mmol/L)	TC (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	AST (μ/l)	ALT (μ/l)	ALP (μ/l)	Y-GT (μ/l)
Control group	0.52 ± 0.08**	2.16 ± 0.39 **	2.31 ± 0.32**	0.32 ± 0.06**	112.7 ± 5.00**	63.74 ± 6.50**	157.29 ± 15.42**	21.89 ± 3.29**
Model group	1.21 ± 0.06	7.40 ± 0.48	1.45 ± 0.25	1.12 ± 0.11	222.94 ± 14.82	96.42 ± 9.79	358.87 ± 21.23	64.63 ± 4.11
Xuezhikang group	0.83 ± 0.06**	3.09 ± 0.46**	2.12 ± 0.23**	0.46 ± 0.09**	147.10 ± 12.75**	70.86 ± 9.53**	185.97 ± 28.71**	35.02 ± 5.49**
High dose group	0.84 ± 0.08**	5.88 ± 0.58**	1.84 ± 0.23**	0.54 ± 0.09**	144.54 ± 12.10**	73.56 ± 7.32**	223.13 ± 17.58**	33.70 ± 4.08**
Middle dose group	0.93 ± 0.06**	6.88 ± 0.53**	1.67 ± 0.13	0.79 ± 0.06**	163.15 ± 17.03**	73.72 ± 5.71**	271.43 ± 28.23**	43.60 ± 6.31**
Low dose group	1.16 ± 0.08	7.19 ± 0.49**	1.56 ± 0.11	0.84 ± 0.09**	196.43 ± 9.42**	84.61 ± 6.13*	283.70 ± 33.32**	49.67 ± 5.44**

($p < 0.01$); compared with the model group, high dose and middle dose lipid-lowering tablets group and Xuezhikang group all significantly decreased liver index of hyperlipidemia rats ($p < 0.01$).

We can see from Table 3, compared with the blank control group, in serum of rats in model group, levels of TG, TC, LDL-C, AST, ALT, ALP and Y-GT significantly increased ($p < 0.01$), the level of HDL-C significantl decreased ($p < 0.01$), showing that hyperlipidemia model was successful (Nawaz et al., 2017). Compared with the model group, high, medium and low dose lipid-lowering tablets group and Xuezhikang group could significantly decrease levels of TC, TG, LDL-C, AST, ALT, ALP, Y-GT ($P < 0.01$, $P < 0.05$) in serum; high dose lipid-lowering tablets group and Xuezhikang group could significantly increase the level of HDL-C ($P < 0.01$).

4. Discussion

The term "blood fat" in modern medicine is like the terms "cream", "fat" in ancient Chinese medicine, according to Magic Pivot, Difference among Metabolic Disorders of Five Body Fluids: Sweat, Urine, Saliva, Tears, Pulp, "Five body fluids from grains synthesize into fat, inward penetrate into the bone hole, upward nourish the brain, and downward flow to the lower body." Zhang Jingyue said: "Five body fluids synthesize into fat to fill the bone hole, pulp the brain, and form the essence of blood." It explains the fat comes from body fluids (Yang et al., 2013). There was no such statement as Hyperlipidemia in ancient medicine. It should belong to the terms in traditional Chinese medicine of "phlegm", "phlegm and blood stasis" and etc (Peng et al., 2014). Hyperlipidemia is due to lipid metabolism disorder in the body, and mainly caused by all kinds of reasons leading to the level of total cholesterol (TC), glycerin three greases (TG) and (or) low density lipoprotein cholesterol (LDL-C) too high, and (or) the level of high density lipoprotein protein cholesterol (HDL-C) too low in plasma or serum, which is an expression of low level systemic lipid metabolism (Liu and Liu, 2010). At the same time, it is also an important factor which leads to many diseases such as atherosclerosis, fatty liver, heart and brain vascular disease (Guo et al., 2011). In addition, hyperlipidemia can increase the severity of necrotizing pancreatitis. At present, with the improvement of human life, hyperlipidemia is still a serious threat to human health with very high incidence. According to statistics from the normal population the incidence rate of hyperlipidemia has been as high as 20–40%, and continue to increase (Yang et al., 2012).

In the replication method of animal model, high fat diet and high fat emulsion gavage method and compound factor method are most commonly used (Sarfraz et al., 2017). High fat diet, in line with human diet due to the characteristics of the formation of hyperlipidemia, is wide applied, but the modeling time in the model replication is very long, Also, due to differences between individual animals and poor uniformity in the selectivity of model index and other aspects, although high fat emulsion gavage method can guarantee the unity of animal individual high fat emulsion intake, which makes up the shortage of feeding high fat forage, the stimulation to animals is large, so animals are in a stressful state for a long time, which affect the results of the experiment (Yan and Song, 2011). Therefore, this experiment was made by using the compound factors of feeding high fat diet and giving fat emulsion by gavage to establish the model of hyperlipidemia in rats (Shen and Song, 2015).

5. Conclusion

The experimental results show that the high, medium and low dose lipid-lowering tablets group could significantly increase the body weight of hyperlipidaemia rats; could significantly decrease the liver index of hyperlipidaemia rats; could significantly decrease levels of TC, TG, LDL-C, AST, ALT, ALP, Y-GT, and significantly increase the level of HDL-C in serum. Also, the effect of lowering blood fat in high dose group was strong. The results of this study provide a scientific basis for the good clinical efficacy of lipid lowering tablets, and lay the foundation for further research of related preparations.

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