THE POTENTIAL EFFECT OF ROSUVASTATIN ON NON ALCOHOLIC STEATOHEPATITIS AND MYOCARDIAL INFARCTION INDUCED IN EXPERIMENTAL RATS

Rezk A. Sanad, Omaima M. Abdallah, Sherif A. Shaltout and Shaymaa H. Ismail.

Department of Pharmacology and Therapeutics, Faculty of Medicine, Benha University

Abstract:

Rosuvastatin (Rsv) is one of statins, which are inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase which inhibit endogenous cholesterol synthesis, possess pleiotropic activities, such as anti-inflammatory, anti-oxidative and antifibrotic effects. Dyslipidemia is an important risk factor for acute coronary syndromes and non alcoholic steatohepatitis (NASH). The present study aimed to investigate the effect of Rsv on myocardial necrosis in an experimental model of acute myocardial infarction (AMI). Animals were given standardized chew supplemented with 2% cholesterol for 4 weeks then AMI was induced by isoprenaline injection (150mg/kg s.c), Rsv was given orally (1mg/kg/day) for 4 weeks before induction of AMI & intraperitoneally (i.p) (10 mg/kg) at the onset of AMI. The obtained result from the current work revealed that pretreatreament with Rsv significantly reduced serum lipid, serum CPK-MB, heart rate, T-wave voltage and myocardial necrosis and significantly increase serum HDL compared to infracted rats. This study also aimed to investigate whether Rsv ameliorate steatohepatitis using a high-fat and high-cholesterol diet-induced rat model. Animals were administered high fat and high-cholesterol diet via oral gavage for 6 weeks, Rsv was administered for 6 weeks (from the start of the study) and from the 6th week to the 10th week from the start of the study (after induction of NASH). The obtained results from the current work revealed that pretreatreament and treatment with Rsv produced significant decrease in serum lipid, ALT and AST, significant increase in serum HDL and improvement of histopathological picture compared to hypercholesterolemic with no medication group. Conclusively, Rsv could have a cardioprotective effect against AMI & improved hepatic steatosis.

Introduction:

Rosuvastatin is the latest of the class of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, this enzyme catalyzes the conversion of HMG-CoA to mevalonate, an early and rate-limiting step in cholesterol biosynthesis. It has the most potent reduction of low-density lipoprotein and elevation of high-density lipoprotein in this class (Guthrie and Martin, 2007). Nonalcoholic fatty liver disease (NAFLD) is a common clinical condition that may progress to non alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma (Bugianesi et al., 2002). NAFLD is the
most common cause of incidental abnormal liver tests and elevated serum liver enzyme activities in the developed world (Angulo, 2002). Obesity, diabetes mellitus, and hyperlipidemia are common components of the metabolic syndrome, which is frequently associated with NAFLD (Marchesini et al., 2005). Since patients with NAFLD are at high risk to develop cardiovascular disease (CVD), statins are frequently prescribed to patients with NAFLD and hyperlipidemia (Nseir et al., 2011). Furthermore, an increased risk of cardiovascular disease (CVD) have been reported in NAFLD patients with type 2 diabetes (Targher et al., 2007). Patient at risk of CVD are prescribed with statin for down-regulating cholesterol production in the liver and increasing the ability of the liver to excrete low-density lipoprotein cholesterol (LDL-C) in the blood, statins are also known to have pleiotropic effects, which seem to be independent of their lipid-lowering action, such as anti-atherosclerotic, anti-inflammatory, anti-thrombosis, and anti-oxidant effects (Calabro and Yeh, 2005 & Liao and Laufs, 2005). These properties could potentially reduce the necrotic area in the setting of AMI. The present study aimed to investigate the effect of rosuvastatin on myocardial necrosis in an experimental model of acute myocardial infarction (AMI). This study also aimed to investigate whether rosuvastatin ameliorate steatohepatitis using a high-fat and high-cholesterol diet-induced rat model.

Material and method:

1-Materials:

A- Drugs and Chemicals:

Rosuvastatin (Rsv): supplied as tablet 10mg (AstraZeneca company, Egypt), Cholesterol: supplied as powder (El-Gomhuria Company, Egypt), Coconut oil: (Zamzam company, Egypt), Isoprenaline HCl: supplied as powder (Sigma, U.S.A.), Urethane: white crystals 0.6 ml/100g of 25% fresh prepared solution. (Prolabo, Paris).

Rosuvastatin was dissolved in saline (McTaggart et al., 2001).

B- Animals

Experimental animals (54 rats weighting 140-240 gm) were kept 6 per cage under complete healthy condition all over the experiment including clean environment, good ventilation and good nutrition. The animals were acclimatized to laboratory conditions for three days before the experiment as for diet, water and temperature (22°C). The work was approved by ethical committee (faculty of medicine, Benha university).
2-Methods:

A-part I: Effect of Rsv on AMI:

To investigate the effect of Rsv on myocardial necrosis in an experimental model of acute myocardial infarction (AMI). 30 male, adult, albino rats will be used in this part. They were divided into 5 groups (n=6 for each) as follows: Group I (control normal rats (N)) was received a standard chow and tap water with no medication. Group II (hypercholesterolemic infarcted group with no medication. (CL)) was received standard chow supplemented with 2% cholesterol (Ivanova et al., 1986) with no medication for 4 weeks before AMI. Group III ( hypercholesterolemic Pre-infarcted treated group (CL+Rsv(Pre-T)) : was received standard chow supplemented with 2% cholesterol with Rsv 1mg/kg/day, oral for 4 weeks before induction of AMI (Dourado et al., 2011). Group IV (hypercholesterolemic infarcted treated group (CL+Rsv (T)): was received standard chow supplemented with 2% cholesterol with Rsv 10 mg/kg/day, i.p at the onset of AMI (Moens et al., 2005). Group V ( hypercholesterolemic pre and infarcted treated group (CL+Rsv (Pre-T+T)): was received standard chow supplemented with 2% cholesterol with Rsv 1mg/kg/day, oral for 4 weeks before induction of AMI and Rsv 10 mg/kg/day, i.p at the onset of AMI.

-Method for induction of myocardial infarction (Marzo and Ghirardi, 1979):

The animals were anaesthetized with urethane in a dose of 1.5-1.75 gm/kg body weight. Half of the dose was injected intraperitoneally, to induce rapid onset and the other half subcutaneously, to insure long maintenance of the anaesthetic effect, the animals were then injected subcutaneously in the abdominal region with freshly prepared solution of the isoprenaline (150 mg/kg).

Biochemical parameters: At the end of the study (after 4 weeks), blood samples (2 ml) were obtained from rats by puncture of the retroorbital sinus, the sinus was punctured and blood entered the capillary tube by its own pressure forming a free flow of blood (Schemer, 1967). Blood was collected into tubes containing EDTA (32 μg.) as an anticoagulant. Plasma was prepared by immediate centrifugation then separated and stored at -20°C to assay the plasma level of serum total cholesterol, triglyceride, LDL, HDL and serum CPK-MB levels was done.

Electrophysiological parameters: The four limbs electrodes were fixed to the animal’s four limbs and records were done using the standard lead II at rate 25 mm/min. E.C.G. tracings were recorded immediately, 30 minutes, 1, 2 and 4 hours after isoprenaline injection. The use of lead II was more informative (in rats) than other leads (Chan et al., 1987).

Histopathological examination: After functional studies were completed, animals were sacrificed, the chest was opened and the heart was excised as a whole, put on cold (8°C) 30 mM KCl to achieve diastolic arrest. Both atria were excised, the ventricles were preserved in neutral formaline 10% and referred for histopathological examination. Heart was sectioned at 5μm and stained with hematoxylin and eosin (H&E). The cardiac sections were examined for the presence of myocyte degenerative changes, infarct like necrosis (Hochman et al. 1987).
**B- Part II: Assessment of the effect of Rsv on NASH:**

24 male albino rats were used, they were divided into 4 groups (n=6 for each) as follows: Group I (control normal rats (N)): was received standard chow and tap water with no medication. Group II (hypercholesterolemic group with no medication (CL)): receive high fat diet via oral gavage for 6 weeks with no medication. Group III (hypercholesterolemic pre-NASH treated group (CL+Rsv (Pre-T))): was received high fat diet via oral gavage for 6 weeks with Rsv 2mg/kg/day, oral (McTaggart, 2003). Group IV (hypercholesterolemic NASH treated group (CL+Rsv (T)): was received high fat diet for 1st 6 weeks with Rsv 2mg/kg/day, oral from 6th week to 10th week from the start of the study (McTaggart, 2003).

**Non alcoholic steatohepatitis(NASH)**

-**Method of induction of non alcoholic steatohepatitis:**

NASH was induced by high-cholesterol diet formed of a balanced laboratory chow in addition to 1% cholesterol and 10% coconut oil via oral gavage for 6 weeks (Yokozawa et al., 2002).

**Biochemical parameters:** At 6th & 10th week from the start of the study, blood samples were drawn by puncture of the retroorbital sinus into non heparinized capillary tubes. Serum was separated by centrifugation for 5 minutes and stored at -20°C to assay the plasma level of total cholesterol, triglyceride, LDL, HDL, ALT and AST.

**Histopathological examination:** At the end of the study (after 10 weeks) animals were sacrificed, the chest was opened, and the liver was excised then fixed in 10% phosphate buffered formalin, fixed specimens were prepared for paraffin sections and staining with H&E (Dury and Wallington, 1967).

**Statistical analysis:**

Data are presented as Mean ± SD. Comparisons between the different groups were carried out using Student’s t-test. Probability (P) values of < 0.05 were considered as statistically significant.

**Results:**

1. **Effect on AMI:**

1.1 **Lipid profile:**

High fat diet supplementation (standard chow supplemented with 2% cholesterol for 4 weeks) resulted in significant rise (P < 0.001) of total cholesterol (203.17 ± 6.43 mg/dl), triglyceride (168.17±5.65 mg/dl), LDL (145.77± 5.77 mg/dl) and significant decrease of HDL (23.67 ± 1.02 mg/dl) in hypercholesterolemic infracted group (group 2) compared to control normal group (Fig.1). Administration of Rsv (1 mg / kg / day oral, 4 weeks
before AMI in group 3 resulted in significant (P < 0.001) reduction in total cholesterol (104 ± 2.86 mg/dl), triglyceride (120.67± 4.08 mg/dl), LDL (51.7±1.87) mg/dl and significant (P <0.05) increase of HDL (28.17 ± 1.05) compared to group 2, while administration of Rsv (10 mg / kg i.p at the onset of AMI) in group 4 produced an insignificant (P >0.05) change in total cholesterol, triglyceride, LDL, HDL compared to group 2. Moreover treatment of hypercholesterolemic rats of group 5 with Rsv (1 mg / kg / day oral, 4 weeks before AMI and 10 mg / kg i.p at the onset of AMI) reduced significantly (P < 0.001) total cholesterol (99.5 ± 3.21 mg/dl), triglyceride (115 ± 2.92 mg/dl), LDL (46.83±3.15 mg/dl) and increased significantly (P <0.05) HDL-c (29.7±1.05 mg/dl) compared to group 2 (Fig.1).

**Figure (1) Histogram showing lipid profile changes in various groups.**

+Significant difference compared to control normal group (1).

#Significant difference compared to hypercholesterolemic infracted group with no medication (group 2).

*Significant difference compared to hypercholesterolemic pre-infarcted treated group (3).

^Significant difference compared to hypercholesterolemic infracted treated group (4).
1.2) ECG changes (Heart rate & T-wave voltage):

Induction of myocardial infarction by isoprenaline injection resulted in significant increase (P < 0.001) in the heart rate and T-wave voltage reaching a maximum level after 4 hours with mean of 468± 6.11 beat/min. & 0.51±0.01 (mV) respectively in group 2 compared to control normal group (Fig.2,3). Administration of Rsv in group 3 & Group 5 resulted in significant decrease (P < 0.001) in the heart rate and T-wave voltage compared to group 2, while administration of Rsv in group 4 resulted in an insignificant change (P > 0.05) in heart rate and T-wave voltage compared to group 2.(Fig. 2,3).

**Figure ( 2 )** Histogram showing heart rate changes at different times in various groups.

+Significant difference compared to control normal group (1).
#Significant difference compared to hypercholesterolemic infarcted group with no medication (2).
*Significant difference compared to hypercholesterolemic pre-infarcted treated group (3).
^Significant difference compared to hypercholesterolemic infarcted treated group(4).
Figure (3) Histogram showing T-wave voltage changes at different times in various groups.

+ Significant difference compared to control normal group (1).

# Significant difference compared to hypercholesterolemic infracted group with no medication (group 2).

* Significant difference compared to hypercholesterolemic pre-infarcted treated group (3).

^ Significant difference compared to hypercholesterolemic infracted treated group (4).

1.3) Serum CPK-MB level:

Induction of myocardial infarction by isoprenaline injection resulted in significant increase (P < 0.001) in serum CPK-MB level with mean of 1211.5±51.54 U/L in group 2 compared to control normal group. Administration of Rsv in group 3 & Group 5 resulted in significant decrease (P < 0.001) in serum CPK-MB level compared to group 2, while administration of Rsv in group 4 resulted in an insignificant change (P > 0.05) in serum CPK-MB level compared to group 2 (Fig. 4).
1.4) **Histopathological examination:**

The heart of control rats showed clear integrity of myocardial membrane, normal cardiac muscle and striations without any infiltration of inflammatory cells. Hypercholesterolemic infarcted group with no medication showed increase of area of degenerative changes in the form of cardiac muscle necrosis with congested blood vessels, interstitial edema. Moreover, hypercholesterolemic pre-infarcted treated group & hypercholesterolemic pre-infarcted and infarcted treated group showed decrease of area of degenerative changes in the form of decrease cardiac muscle necrosis, decrease congested blood vessels and decrease interstitial edema, while hypercholesterolemic infarcted treated group showed increase of area of degenerative changes in the form of cardiac muscle necrosis with congested blood vessels, interstitial edema.
2. Effect on NASH:

2.1) Lipid profile at the 6th week:

High fat diet supplementation (1% cholesterol and 10% coconut oil) for 6 weeks resulted in significant rise (\( P < 0.001 \)) of total cholesterol (212.3 \(\pm\) 7.7 mg/dl), triglyceride (176.7 \(\pm\) 4.4 mg/dl), LDL (155 \(\pm\) 7.3 mg/dl) and significant decrease of HDL (22 \(\pm\) 1.0 mg/dl) in hypercholesterolemic infracted group compared to control normal group (Fig.5). Administration of Rsv (2 mg / kg / day, oral for 6 weeks in group 3 resulted in significant (\( P < 0.001 \)) reduction in total cholesterol (106.7 \(\pm\) 2.9 mg/dl), triglyceride (127.2 \(\pm\) 3.1 mg/dl), LDL (54.2 \(\pm\) 2.5) mg/dl and significant (\( P < 0.05 \)) increase of HDL (27 \(\pm\) 1.1) compared to group 2 (Fig.5). Rats in group 4 fed on high fat diet without treatment for 6 weeks resulted in insignificant (\( P > 0.05 \)) change in total cholesterol, triglyceride, LDL, HDL compared to group 2 (Fig.5).

2.2) Lipid profile at the 10th week:

Group 2 on standard chew without medication from 6th week to 10th week from the start of the study was still significantly (\( P < 0.001 \)) higher in total cholesterol (193.3 \(\pm\) 6.2 mg/dl), triglyceride (161 \(\pm\) 3.3 mg/dl), LDL (136 \(\pm\) 6.1 mg/dl) and less in HDL (25.2 \(\pm\) 1.0) compared to control normal group. (Fig.5). Group 3 on standard chew without medication from 6th week to 10th week from the start of the study still show significant (\( P < 0.001 \)) reduction in total cholesterol (104.2 \(\pm\) 3.4 mg/dl), triglyceride (113 \(\pm\) 4.3 mg/dl), LDL (52.9 \(\pm\) 1.98 mg/dl) and rise in HDL (28.8 \(\pm\) 0.9) compared to group 2 (Fig.5). Group 4 on standard chew with Rsv (2 mg/kg/day from 6th week to 10th week from the start of the study, oral) resulted in significant (\( P < 0.001 \)) reduction in total cholesterol (112 \(\pm\) 1.4 mg/dl), triglyceride (123 \(\pm\) 2.5 mg/dl), LDL (57.8 \(\pm\) 2.7) mg/dl and significant (\( P < 0.05 \)) increase of HDL (29.6 \(\pm\) 1.0) compared to group 2 (Fig.5).
2.3) Liver functions at the 6th week:

High fat diet supplementation (1% cholesterol and 10% coconut oil) for 6 weeks resulted in significant rise (P < 0.05) & (P < 0.001) of AST (91.3± 7.5 u/l) and ALT (53.5± 2.4 u/l) respectively in group 2 compared to control normal group (Fig.6). Treatment of hypercholesterolemic rats of group 3 with Rsv (2 mg /kg /day ,oral, for 6 weeks) significantly reduced (P < 0.05) AST ( 68.5± 5.5 u/l) and significantly (P < 0.001) reduced ALT ( 35.3±1.3 u/l ) compared to group 2 (Fig.4). Moreover, rats in group 4 fed on high fat diet without treatment for 6 weeks resulted in insignificant change (P >0.05) in AST & ALT compared to group 2 (Fig.6).

2.4) Liver functions at the 10th week:

Group 2 on standard chew without medication from 6th week to 10th week from the start of the study was still significantly (P < 0.001),(P < 0.05) higher in AST (86±4.5u/l ) & ALT (48.5±2.0 u/l ) respectively compared to control normal group (Fig.6). Group 3 on
standard chew without medication from 6\textsuperscript{th} week to 10\textsuperscript{th} week from the start of the study sill show significant (P < 0.05), (P < 0.001) respectively reduction in AST (62.3±3.2 u/l) & ALT (33.5±2.2 u/l) compared to group 2. (Fig.6). Group 4 on standard chew with Rsv (2 mg/kg/day, oral, from 6\textsuperscript{th} week to 10\textsuperscript{th} week from the start of the study) resulted in significant (P < 0.05), (P <0.001) reduction in AST (58.2 ± 4.7 u/l) & ALT (31.8±1.1 u/l) respectively compared to group 2 (Fig.6).

\textit{Figure (6): Histogram showing variations in the mean levels of SGOT (AST) & SGPT (ALT) in various groups at 6\textsuperscript{th} & 10\textsuperscript{th} week.}

+Significant difference compared to control normal group (1).

#Significant difference compared to hypercholesterolemic group with no medication (group 2).

2.5) Histopathological results:

The liver of normal rats showed normal hepatic architecture with normal central vien, normal portal tract and normal hepatocyte with normal sinusoids inbetween. Hypercholesterolemic non treated group showed lobular inflammation, hydrobic degeneration of the hepatocyte, inflammatory cell infiltration in the portal tract and steatosis. Both hypercholesterolemic pre-treated group & hypercholesterolemic treated group showed decrease lobular inflammation, decrease hydrobic degeneration of the hepatocyte, decrease inflammatory cell infiltration in the portal tract and no steatosis.
Discussion:

Rosuvastatin is a lipid-lowering agent that competitively inhibits the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Rosuvastatin exhibits the highest efficacy in the reduction of LDL cholesterol, total cholesterol and triglycerides compared with other statins at comparable doses (Vijan and Hayward 2004). The present study showed that pretreatment with Rsv (4 weeks before infarction) significantly reduced heart rate, t-wave voltage compared to hypercholesterolemic infarcted rats. These data are supported by previous studies revealed that Statins improve myocardial functions and reducing myocardial infarct size in rats (Efthymiou et al., 2005). Our findings have demonstrated that pretreatment of hyperlipidemic infarcted rats with Rsv (4 weeks before infarction) significantly lowered the leakage of the cardiac biomarkers (CPK_MB level), such observations could be attributed to the potential role of Rsv in protecting the myocardial membranes and in alleviating the extent of myocardial damage. In addition, the histopathological changes of pretreated groups showed retardation of inflammation and myonecrosis which could be attributed also to the antioxidant and anti-inflammatory properties of rosuvastatin. These data are supported by previous studies (Kannan and Quine, 2011 & Dubé, 2014) revealed that statins improve myocardial functions and reducing myocardial infarct size in rats. The present study showed that pretreatment with Rsv (4 weeks before infarction) significantly reduced total cholesterol, triglycerides, LDL and significantly increased HDL. The obtained data are in harmony with previous studies (Cheng, 2004 & Kipshidze and Kapanadze, 2008 & Yoshino et al., 2009 & Koksal et al., 2011) concluded that statin significantly reduced total cholesterol, triglycerides, LDL and significantly increased HDL. Hypocholesterolemic effect of Rsv is mainly mediated via HMG-CoA reductase inhibition (Cheng-Lai, 2002 & Kannan and Quine, 2013). Despite the molecular biological activities of statins, which clearly show anti-inflammatory and antioxidant effects, the results of two randomized trials evaluating rosuvastatin failed to show a reduction in cardiovascular events (Kjekshus et al., 2007). The present study also showed no significant change in myocardial injury in hypercholesterolemic infarcted rats when was given immediately after the onset of AMI. These results are in agreement with several studies (Jones et al., 2002 & Ikeda et al., 2003) that revealed that Rsv given immediately at the onset of infarction insignificantly improved myocardial necrosis in experimentally induced model of myocardial infarction.

The exact mechanisms by which Rsv prevent myocardial necrosis are beyond the scope of our study. But it has been established by the work of others. According to Davignon and Laaksonen, 1999; statins have several effects related to the reduction of LDL-C levels. Rosenson and Tangney, 1998; have suggested 4 non-lipidic mechanisms that may contribute to the beneficial effects on clinical events. These effects include modification of endothelial function, inflammatory response, plaque stabilization, thrombus formation and other effects as anti-atherosclerotic, anti-inflammatory, anti-thrombosis, and anti-oxidant effects (Robinson et al., 2005 & John et al., 2005). In this study, we also assessed the beneficial effect of Rsv on the progression of NAFLD in two
major manifestations of liver disease, that are, steatosis and inflammation. The present study showed that pretreatment with rosuvastatin (for six weeks) lead to a significant decrease of serum AST, ALT, total cholesterol, triglyceride, LDL and significantly increased HDL. These results are in agreement with several studies (Browning, 2006 & Ekstedt et al., 2007 & Fraulob et al., 2012) that have already shown that statins can decrease serum lipid and aminotransferase levels; to confirm this finding, liver sections were evaluated for lobular inflammation. Rsv reduce lobular inflammation in the pretreated group, this is in agreement with (Okada et al., 2013). The present study showed that treatment with Rsv (for 4 weeks after induction of NASH) lead to significant reduction of total cholesterol, triglyceride, LDL, significant increase of HDL and reduction of lobular inflammation in the treated group compared to hypercholesterolemic non treated group. These result are in agreement with (Svegliati-Baroni, et al. 2006 & Neto-Ferreira et al. 2013) that reported that administration of Rsv decreased the liver steatosis, and improved the circulating levels of cholesterol and triglycerides. The present study showed that treatment with Rsv (for 4 weeks after induction of NASH) lead to a significant improvement in AST, ALT compared to hypercholesterolemic non treated group. These finding are in line with other studies (Kargiotis et al., 2014) that reported that Rsv significantly reduce serum AST, ALT level. The results found in this study were partially in contrast to those of Neto-Ferreira et al., 2013 who did not find a significant reduction of AST, while there were an amelioration of lipid profile, ALT, liver histopathological changes induced by Rsv. This work did not examine the mechanism by which Rsv ameliorated NASH. But it has been established by the work of others who revealed statins have been reported to have immunomodulatory, antioxidative, antithrombotic actions, as well as an antibacterial action (Nseir et al., 2012). Since inflammatory and oxidative mechanisms are involved in the pathogenesis of NASH, statins have been proposed as therapy for patients with NASH.

**Conclusion**

The result of this study revealed that Rsv had protective effect against AMI which is proved by reduction of serum CPK-MB level, myocardial function and myocardial necrosis in RSV pre-treated group in comparison with infarcted rats. RSV also ameliorated high-fat and high-cholesterol diet-induced NASH which is proved by reduction of elevated serum ALT and AST with improvement of histopathological picture in Rsv treated groups in comparison with non treated group.

**Reference:**


التأثير الدوائي المحتمل لعقار الروسوفاستاتين على الاحتشاء الحاد في عضلة القلب والتهاب الكبد الدهني

المحدث تجريبيا في فئران التجربة

رزق أحمد سند - أميمة محمد عبد الله - شريف أحمد شلتوت - شيماء هارون إسماعيل
قسم الفarmacولوجيا الأكينيكة - كلية طب بنها - جامعة بنها

يتبع الروسوفاستاتين مجموعة الشتاتين (مثبطات أنسيم هيدروكسي ميثيل كو ايه)، التي تقل صناعة الكوليسترول داخل الجسم، وочно ما هي نشاطات متعددة كمضاد للالتهابات ومضادة للأكسدة ومضادة للتلف، وحيث أن ارتفاع نسبة الدهون في الدم من أهم العوامل المسببة لأمراض الشرايين التاجية الحادة، ومرض التهاب الكبد الدهني غير الكحولي، فإن استخدام الروسوفاستاتين في هذه الحالات له قيمة كبيرة. ولقد صممت هذه الدراسة لحث دراسة فاعلية عقار الروسوفاستاتين في الوقاية والعلاج من الاحتشاء الحاد في عضلة القلب المحدث تجريبيا في فئران التجربة، وقد تم إضافة 2% كوليسترول لطعام الفئران لمدة أربعة أسابيع لرفع مستوى الكوليسترول، ثم اعطاء جلطة قلبية عن طريق حقن عقار الأزوبيسينين (150 مجم/كجم بحث الجم) وضعه روسوفاستاتين (2 مجم/كجم يوم) بالفق، لمدة أربعة أسابيع قبل إحداث الجلطة (10 مجم/كجم بالحقن في الغشاء الوركي) عند احداث الجلطة، ولقد أوضحت النتائج في هذا العمل أن استخدام الروسوفاستاتين لمدة أربعة أسابيع قبل احداث الجلطة له تأثير ذو مداة إحصائية في خفض مستوى الكوليسترول والدهون الثلاثية والبروتينات الدهنية ذات الكثافة المنخفضة، لارتفاع مستوي البروتينات الدهنية ذات الكثافة المرتفعة، وانخفاض مستوي الكولسترول في مرحلة الدهون. وفي الدراسة أيضا لدراسة دور عقار الروسوفاستاتين في الوقاية من حدوث وتظاهر مرض التهاب الكبد الدهني غير الكحولي المحدث تجريبيا في فئران التجربة، وقد تم استخدام التهاب الكبد الدهني غير الكحولي تجريبيا ب استخدام غذاء عادي الدهون والكوليسترول لمدة 6 أسابيع، ثم اعطاء عقار الروسوفاستاتين (2 مجم/كجم/اليوم) لمدة أسبوع، بدأ العمل في دراسة (2 مجم/كجم/اليوم) لمدة أسبوع، وانتهت بابس العقدة، بعد انتهاء الدراسات ولح الاسبوع العاشر من بداية الدراسة (بعد انتهاء التهاب الكبد الدهني غير الكحولي).

ولقد أوضحت النتائج في هذا العمل أن استخدام الروسوفاستاتين قليل و بدأ افتراض التهاب الكبد الدهني غير الكحولي له تأثير ذو مداة إحصائية في خفض مستوى الكوليسترول والدهون الثلاثية والبروتينات الدهنية ذات الكثافة المنخفضة، وارتفاع مستوى البروتينات الدهنية ذات الكثافة المرتفعة، وانخفاض مستوي الدهون، أيضا كان له دور في تقليل حدوث التغيرات الخلوية المصاحبة داخل الكبد.