SUMMARY & CONCLUSION

Myocardial infarction is serious disease accompanied by abnormal changes in cardiovascular measures in the form of increased heart rate, ST segment elevation and increased CPK-MB level.

Insulin resistance is a major pathological change observed in patients with ischemic heart disease, Improvement of insulin resistance may play an important role in preventing atherosclerosis in diabetic patients with hyperlipidemia.

Atorvastatin is (HMG-CoA) reductase inhibitor plays an important role in improving myocardial infarction and glucose metabolism.

Pioglitazone is athiazolidinedione with peroxisome prolifirator-activated receptor-γ agonist activity improved insulin resistance and prevented the development of atheroscelerosis in animal models and reduced mortality of myocardial infarction and stroke.

The present study was carried out to study the effect of these drugs on acute myocardial infarction (AMI) in diabetic and non diabetic rats and insulin resistance induced in experimental albino rats. Also in vitro studies were done to investigate effects of these drugs on isolated rabbit's heart and aorta.

To study effect on AMI in non diabetic rats, 30 male albino rats were classified into 5 equal groups (6 rats in each group). First group which is control group. AMI was induced in all other groups by isoprenaline 150 mg/kg S.C. injection in anterior abdominal wall. 2nd group was not pre-treated , 3rd group pre-treated with atorvastatin 10 mg/kg I.P injection 2

hours before isoprenaline, 4th group pretreated with pioglitaone 10 mg/kg I.P injection 2 hours before isoprenaline and 5th group pretreated with both drugs 10 mg/kg from each drug I.P injection 2 hours before isoprenaline. All these groups were subjected to measuring heart rate, ST segment elevation, serum CPK-MB fraction and histopathological study for left ventricle 4 hours after isoprenaline.

Data obtained in the present study pointed out that pretreatment of isoprenaline induced AMI in male albino rats with atorvastatin and/or pioglitazone leads to significant improvement in parameters of AMI as regard heart rate, ST segment elevation , CPK-MB and histopathology.

Pioglitazone is as significant as the combined drugs in most of these parameters.

To study effect on AMI in diabetic rats, 30 male albino rats were classified into 5 equal groups (6 rats in each group). Diabetes was induced by administration of 10% of l-fructose in drinking water for 8 weeks. AMI was induced in all other groups by isoprenaline 150 mg/kg S.C.injection in anterior abdominal wall. First group which is control diabetic group. 2nd group was not pre-treated , 3rd group pre-treated with atorvastatin 10 mg/kg I.P injection 2 hours before isoprenaline, 4th group pretreated with pioglitaone 10 mg/kg I.P injection 2 hours before isoprenaline and 5th group pretreated with both drugs 10 mg/kg from each drug I.P injection 2 hours before isoprenaline. All these groups were subjected to measuring heart rate, ST segment elevation, serum CPK-MB fraction and histopathological study for left ventricle 4 hours after isoprenaline.

Data obtained in the present study pointed out that pretreatment of isoprenaline induced AMI in male albino rats with atorvastatin and/or pioglitazone lead to significant improvement in parameters of AMI as regard heart rate, ST segment elevation , CPK-MB and histopathology.

Pioglitazone is as significant as the combined drugs in heart rate and CPK-MB level but in ST segment elevation atorvastatin is as pioglitazone but combination is more significant.

Histopathology indicates that in infracted non diabetic rats pioglitazone pre-treated group had the little signs of acute infarction ,followed by the combination (atorvastatin+pioglitazone) pre-treated group. But atorvastatin pre-treated group showed the most evident signs of acute infarction.

While in infracted diabetic rats combination (atorvastatin+pioglitazone) pre-treated group had the little signs of acute infarction ,followed by pioglitazone pre-treated group. But atorvastatin pre-treated group showed the most evident signs of acute infarction.

As regard effect of these drugs in insulin resistance, 30 male albino rats were classified into 5 equal groups (6 rats in each group).The first group is control, Insulin resistance was induced by administration of 10% of l-fructose in drinking water for 4 weeks. . 2nd group was not treated , 3rd group treated with atorvastatin 10 mg/kg p.o for 2 weeks, 4th group treated with pioglitaone 10 mg/kg p.o for 2 weeks and 5th group treated with both drugs 10 mg/kg from each drug p.o for 2 weeks. All these groups were subjected to measuring blood pressure, lipid profiles(total cholesterol,

triglycerids, HDL-C and LDL-C) plasma insulin level, plasma glucose level and HOMA IR index.

Data obtained in the present study pointed out that treatment of experimentally - induced insulin resistance in male albino rats with atorvastatin and/or pioglitazone leads to significant improvement in parameters of insulin resistance such as blood pressure, lipid profiles(total cholesterol, triglycerids, HDL-C and LDL-C) plasma insulin level, plasma glucose level and HOMA IR index.

Concerning blood pressure treated groups showed significant reduction from the diseased non treated group, but they are not significantly different from each other. All other parameters pioglitazone was as significant as the combination of both drugs except for LDL-C the combined drugs were more significant.

In vitro studies on isolated perfused rabbit heart revealed that both drugs had no action on isolated rabbit heart.

In vitro studies on isolated rabbit aortic strip revealed that pioglitazone lead to significant relaxation in noradrenaline precontracted isolated rabbit aortic strip may be through action on releasing endothelial nitric oxide. Atorvastatin had no action on isolated rabbit aortic strip.

From previous data one may assume that (conclusions):

- Atorvastatin and/or pioglitazone prophylactic treatment improved the produced pathological changes produced in acute myocardial infarction.
- Both drugs are usefull and effective in managing insulin resistance.
- Pioglitazone showed superiority over that of atorvastatin particularily in improvement of insulin resistance and lipid profiles.
- Combination of both drugs is effective to reduce LDL-C and abnormal ECG changes in cases of diabetes.

Proposal for future research:

The protective and therapeutic effects of atorvastatin and pioglitazone, their possible mechanisms of action, and the appropriate dose levels should be studied further.