Some Aspects of Vascular Dysfunction Associated with Experimentally Induced Diabetes in Adult Laboratory Albino Rats

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SUMMARY

This work reveals the impact of chronic high blood glucose (which is known as diabetes) on the state of blood vessels, by narrowing them and thus reducing the transportation of blood to organs causing malfunctions.

In this work,adiabetic patient model was prepared from male albino rats by injecting Streptozotocinin primary dose; 27.5 mg per kilogram of body weight, followed by four booster weekly doses; 11.25 milligrams per kilogram of body weight. This model wasdiabetic after 45 (forty five) days since injecting Streptozotocin primary dose.

This model showed the symptoms of diabetes and its complications, as increasing blood glucose level to more than three times the normal level, the appearance of glucose in urine, yellowing of falling hair color, and decreased body weight resulting from the lipolysis of body fats to fatty acids that released into blood plasma causing its greasing.

Fatty acids replace glucose as a source for generating mitochondrial ATP molecules in the cell, and consequently, massive amounts of triglycerides, lipoproteins and cholesterol are formed in the blood.

During cycling of LDL cholesterol in blood circulation, it binds to the phospholipids in the cellular plasma membrane of endothelium lining the blood vessels, which in turn, loses smoothness and becomes rough and fit to entrapping the suspended solids in the blood circulation leading to blood vessels narrowing and may be clogged due to increasing hardening of blood vessels walls, which lose their flexibility and their power to broaden when necessary, as in the case of increasing heart beat for instance.

Manifestations of blood vessel narrowing were revealed clearly in small vessels and capillaries. Complete blockage may take place, and consequently lack in plasma in intercellular spaces depriving cells from their vital sources especially the oxygen, and finally suffocation of these cells may take place, causing malfunctions in different tissues and organs where these suffocated cells are present.

The research dealt with different drugs according to their impact mechanism, some of them are to counter the causes of harmful lipids formation, others are curative agents for blood vessels walls converting them to the normal case, and the last group of proposed drugs dealt with the volume of circulating blood.

The goal of experimenting these proposed drugs is to improve the organ tissue cells blood supply which assured by measuring the functional markers of body organs using blood samples, as well as measuring the extent of improvement in the absorptive ability of the tissues in terms of rectus abdominus muscle preparation after treatment.

The first drug group:

This group counters the causes of harmful lipids, from this group:

1 - Pravastatin sodium (Lipostat) drug: It addresses the causes of total blood cholesterol, LDL cholesterol and also Tri-glycerides. The used dose was 0.9 mg/kg of rat body weight derived from the particular human dose of 0.143 mg/kg human body weight.

2 - Essential forte:which is dietary supplement drug for basic phospholipids, it contributes to providing the body witha phospholipids source, which in turn contribute to the renewal of tissue cells, especially liver tissue, as well as converting neutral fats and cholesterol (especially LDL cholesterol) to the form that can be transferred and becomes fit to combustion.If this is not the case, low-density cholesterol in blood circulation would bind to the phospholipids in the plasma membrane of endothelium lining the blood vessels, which in turn, loses smoothness and becomes rough and fit to entrapping the suspended solids in the blood circulation leading to blood vessels narrowing. The used dose was twice

daily (27.0 mg/kg of rat body weight derived from the particular human one daily of 4.28 mg/kg human body weight/ one daily dose).

The second drug group

This group addresses the consequences of high blood pressure inside the blood vessels. These drugs include:

1- Amolodipinebesylate (Norvasc):is adrug which inhibits pumping of calcium ions across the membranes of heart muscle and smooth muscle of blood vessels including coronary vessels. The used dose was 0.9 mg/kg of rat body weight derived from the particular human dose of 0.143 mg/kg human body weight.

2- Fosinopril sodium – hydrochlorothiazide: These drugs reduce the pressure inside the arteries by reducing compression of their walls, and lead to non-reabsorption of water from initial urine and hence blood volume within the blood vessels will not increase, and consequently the capillaries will not burst. This effect is primarily due to the factthat these drugs inhibit Renin hormone,which converts angiotensin I into angiotensin II. The used dose was 0.9 mg/kg of rat body weight derived from the particular human dose of 0.143 mg/kg human body weight.

The following is a summary of the results of the impact of drugs used in the experiment on the levels of markers of organs functions, such as liver, kidney using blood samples of the animals:

A– The effect of Pravastatin sodium (Lipostat) on the following parameters:

1-Serum glucose levels: The data showedinsignificant differences in comparison with diabetic control group.

2- Serum total cholesterol : The results obtained from analysis in case of*Pravastatin* sodium showed highly significant decrease.

3- Serum HDL Cholesterol Levels : Pravastatin sodium treated rats showed highly significant increase in the values.

4- Serum LDL Cholesterol Levels: Values of LDL Cholesterol showed highly significantreduction against the levels recorded in rats of diabetic control group.

5- Serum Triglycerides Levels: The results obtained from the analysis of serum triglycerides (TG) in rats treated withPravastatin sodiumshowed highly significant decrease in the data in comparison with diabetic control group.

6- Blood glycosylated hemoglobin (HbA1c): Data revealed that highlysignificant decrease in level in comparison to the levels recorded in rats of diabetic control group.

7- Liver functions:

a) ***Serum Alanine Aminotransferase (sALT).***Data revealed that Alanine aminotransferase (ALT), levels were highlysignificant decreased in level in comparison to the levels recorded in rats of diabetic control group.

b) ***Serum Aspartate aminotransferase (sAST).***The results obtained from the analysis of serum AST activity showedsignificant decrease in comparison to the levels recorded in diabetic control group rats.

8-Kidney functions:-

a) ***Blood Urea Nitrogen (BUN).***Blood urea nitrogen analysis of Pravastatin sodium rats group showed highlysignificant reduction in BUN in comparisonto the control diabetic group.

b)*Serum Creatinine.*The data obtained from serum creatinine analysis showed highly significantreduction in its level as compared to the levels recorded in diabetic rats control group.

9- Bio-assay:Glucose uptake by rectus abdominus muscle. The results obtained from the analysisshowed significancedifferences in comparison with diabetic control group.

B – The effect of dietary supplement drug(Essential forte) on the following parameters:

1- Serum glucose levels: The results of analysis showedinsignificant differences in comparison with diabetic control group.

2-Serum total cholesterol: The data obtained from analysis showed highly significant reduction.

3- Serum HDL Cholesterol Levels: Essential forte drugtreated rats showed highly significant increase in the values.

4- Serum LDL Cholesterol Levels: Values of LDL Cholesterol showed highly significantreduction against the levels recorded in rats of diabetic control group.

5- Serum Triglycerides Levels: The results obtained from the analysis of serum triglycerides (TG) in rats treated withEssential forteshowed highly significant decreasein comparison with diabetic control group.

6- Blood glycosylated hemoglobin (HbA1c): Data revealed that highlysignificant decrease in level in comparisonto the levels recorded in rats of diabetic control group.

7- Liver functions:

a. ***Serum Alanine Aminotransferase (sALT).***Analysis of data revealed that Alanine aminotransferase (ALT), levels were highlysignificant decrease in level in comparisonto the levels recorded in rats of diabetic control group.

b. ***Serum Aspartate aminotransferase (sAST).*** The results obtained from the analysis of serum AST activity showedsignificant decrease in comparison to the levels recorded in diabetic control group rats.

8-Kidney functions:-

a) ***Blood Urea Nitrogen (BUN).*** Analysis of Essential forte datashowed highlysignificant reduction in BUN in comparisonto the control diabetic group.

b) ***Serum Creatinine.*** The data obtained from serum creatinine analysis showed highly significantreduction in its level compared to the levels recorded in diabetic rats control group.

9- Bio-assay:Glucose uptake by rectus abdominus muscle. The results obtained from the analysisshowed significancedifferences in comparison with diabetic control group.

C– The effect of Amlodipine besylate drug (Norvasc) on the following parameters:

1-Serum glucose levels: The results of analysis showedsignificant differences in comparison with diabetic control group.

2-Serum total cholesterol : The data obtained from analysis showed insignificant differences in comparison with diabetic control group.

3-Serum HDL CholesterolLevels: Amlodipine besylate drugtreated rats showed insignificant differences in the data.

4- Serum LDL Cholesterol Levels: Values of LDL Cholesterol showed insignificant differences against the levels recorded in rats of diabetic control group.

5- Serum Triglycerides Levels: The results obtained from the analysis of serum triglycerides (TG) in rats treated withAmlodipine besylateshowed insignificant differences in the data in comparison with diabetic control group.

6-Blood glycosylated hemoglobin (HbA1c): Data revealed that highlysignificant decrease in level in comparisonto the levels recorded in rats of diabetic control group.

7-Liver functions:

a) ***Serum Alanine Aminotransferase (sALT).***Analysis of Amlodipine besylate group data revealed that Alanine aminotransferase (ALT), levels were highlysignificant decrease in level in comparisonto the levels recorded in rats of diabetic control group.

b) ***Serum Aspartate aminotransferase (sAST).***The results obtained from the analysis of serum AST activity showedsignificant decrease incomparison to the levels recorded in diabetic control group rats.

8-Kidney functions:-

a*) Blood Urea Nitrogen (BUN).*Analysis of Amlodipine besylatedatashowed highlysignificant reduction in BUN in comparisonto the control diabetic group.

b) *Serum Creatinine.*The data obtained from serum creatinine analysis showed highly significantreduction in its level compared to the levels recorded in diabetic rats control group.

9- Bio-assay:Glucose uptake by rectus abdominus muscle. The results obtained from the analysisshowed significancedifferences in comparison with diabetic control group.

D – The effect of Fosinopril sodium- hydrochlorothiazide on the following parameters:

1-Serum glucose levels: The results of analysis showedinsignificant differences in comparison with diabetic control group.

2- Serum total cholesterol : The data obtained from analysis showed highly significant reduction.

3-Serum HDLCholesterol Levels: Fosinopril sodium- hydrochlorothiazide group showed highly significant increase in the values.

4- Serum LDL Cholesterol Levels: Values of LDL Cholesterol showed highly significantreduction against the levels recorded in rats of diabetic control group.

5- Serum Triglycerides Levels: The results obtained from the analysis of serum triglycerides (TG) in rats treated withFosinopril sodium- hydrochlorothiazide drug showed highly significant decrease in the data in comparison with diabetic control group.

6-Blood glycosylated hemoglobin (HbA1c): Data revealed that highlysignificant decrease in level in comparisonto the levels recorded in rats of diabetic control group.

7-Liver functions:

a) Serum Alanine Aminotransferase (sALT).Analysis of data revealed that Alanine aminotransferase (ALT), levels were highly significant decrease in level in comparisonto the levels recorded in rats of diabetic control group.

b) Serum Aspartate aminotransferase (sAST). The results obtainedfrom the analysis of serum AST activity showedsignificant decrease in comparisonto the levels recorded in diabetic control group rats.

8-Kidney functions:-

a) Blood Urea Nitrogen (BUN).Analysis of datashowed highlysignificant reduction in BUN in comparisonto the control diabetic group.

b) ***Serum Creatinine.***The data obtained from serum creatinine analysis showed highly significantreduction in its level compared to the levels recorded in diabetic rats control group.

9-Bio-assay:Glucose uptake by rectus abdominus muscle. The results obtained from the analysisshowed significancedifferences in comparison with diabetic control group.

The results were statistically analyses by **(ANOVA)** with the determination of least significant difference test (LSD) at conventional probability levels ($P< 0.05$).

In the following two pages (97) and (98) two figures are presented demonstrating the percentage differences of the all parameters of all groups of the experiment.