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RESEARCH ARTICLE

Influence of oral hypoglycemic agent (Glibenclamide)on Biochemical parameters.

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Abstract

Objective: In vivo study was carried out to investigate the effect of oral glibenclamide on biochemical laboratory findings.
Methods: 30 subjects (17 males and 13 females) with an average age of (45 ±16 years) and average weight (80 ± 18 kg) were participated in this study. They were newly diagnosed with non-insulin dependent diabetes mellitus. 20 healthy volunteers of comparable age and weight (47 ± 13 years ; 77 ± 12 kg) were used as control sample. Two venous blood samples were taken from each subject, first blood sample was taken before glibenclamide therapy (5 mg/daily) and the second blood sample was taken 14 weeks after drug therapy. The two samples were analysed for glucose, HbA1c, total cholesterol, Triglyceride, LDL and HDL.
Results: At week 14, glibenclamide treatment resulted in significantly greater reduction in both HbA1c and fasting plasma glucose ($p < 0.05$). Triglyceride as well as HDL were significantly increased.
Conclusion: glibenclamide treatment for 14 weeks is effective in reducing significantly fasting blood sugar and HbA1c and it has positive effect in raising the level of HDL.

Introduction:-

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, defective insulin action or both. Diabetes may cause many complications, such as increased risk of blindness, kidney failure, heart attacks, and stroke (Sona et al 2009). It's a well-known fact that cardiovascular disease is a leading cause of both morbidity and mortality in diabetic patients (Omonkhelin et al. 2011). Type 2 diabetes is closely associated with dyslipidemia, obesity and characterized by initial phases of progressive insulin resistance and sedentary life style, unhealthy dietary-habit (Manjusha et al. 2011).Glibenclamide is a potent sulfonylurea which is administered orally in small doses in the management of type 2 diabetes mellitus (Vitthal et al. 2014). Sulfonylurea agent causes stimulation of pancreatic beta cells leading to the release of insulin and causes hypoglycemia (Waller and Renwick. 1994). Glibenclamide is the first line option for treating type 2 diabetes in people who are not overweight (Katzung. 2001). Vitthal et al. (2014) reported that Glibenclamide showed significant reduction in fasting and postprandial blood glucose after 4 and 8 weeks of treatment. The pharmacological treatment of hyperglycemia in most type 2 diabetes patients begins with low doses of sulphonylurea, metformin or glucose inhibitors (Pravinkumar and Talele. 2012). The physician should review each of the drug option and learn the benefits of each drug against cost, contraindications, case of compliance, duration of action, patient's weight and lipid profile (Duckworth et al. 2003). Diabetic patients that received only glibenclamide, showed significant reduction in the blood glucose level (Omonkhelin et al. 2011; Mori et al. 2012).Diabetic dyslipidaemia is characterized by an increase in triglycerides (TG), a decrease in HDL cholesterol and an increase in small dense LDL particles (Reyadh 2012).Combination therapy for diabetic patients usually refers to the use of oral antidiabetic agents together with a single injection of intermediate acting insulin at bed time (Vitthal et al. 2014). Sona et al. (2009) found that regularization of the insulin dose and 3 months treatment with using sulphonylurea and metformin days caused significant decrease in fast blood sugar, total cholesterol,

triglyceride and LDL. The use of metformin / glyburide combination or metformin alone in the treatment of type 1 diabetes significantly maintained lipid profile at levels closer to that of non-diabetic controls ((Reyadh 2012). Pravinkumar and Talele. (2012) have found that diabetic patients receiving two combination treatment of metformin with glimepiride and glibenclamide had significant decrease in lipid profile by decreasing their LDL and same time increasing HDL.

In the present study the effects of Glibenclamide on glucose, HbC1A level and lipid profile was investigated. This study will provide information about the ability of this drug to reducing atherosclerosis and hence reducing cardiovascular complications, frequently associated with type 2 DM.

Material and Methods:-

In vivo study:-

This study was conducted on 30 patients (17 males and 13 females). With an average age (45 ±16 years) and average weight (80 ± 18 kg). The patients were newly diagnosed with diabetes mellitus of type 2 in the outpatient clinic of Jordan hospital. The patients were on glibenclamide therapy (5mg/day). 20 healthy volunteers of comparable age and weight (47 ± 13 years; 77 ± 12 kg) were used as control sample.

Blood samples:-

Two venous blood samples were taken from each subject, first blood sample was taken before glibenclamide therapy (5 mg/daily) and the second blood sample was taken 14 weeks after drug therapy. All blood samples were left to clot and were centrifuged at 3500 rpm for 10 minutes. Serum was obtained from each sample and was used to measure glucose, HbA1c, total cholesterol, Triglyceride, LDL and HDL.

Biochemical parameters determination:-

All kits used to measure the biochemical parameters were purchased from Randox laboratories. Ltd; UK). Glucose, total cholesterol (T.Chol) triglyceride (TG), LDL and HDL were measured according to the procedure of Burtis et al. (2014). A method of Hong and Richard (2013) was used to determine the Percent HbA1c.

Result:-

The effect of antidiabetic agent (Glibenclamide) on in vivo laboratory findings are listed in table 1. All the patients enrolled in this study were assigned to receive glibenclamide5 mg/day for 14 weeks.

Significant reduction ($p < 0.05$) in fasting blood glucose level (129.5 ± 4.5 mg/dl) was observed in treated patients when compared with values before treatment (175.6 ± 10.1 mg/dl). Table 1 shows a decrease in mean HbA1C during the study. After 14 weeks of glibenclamide therapy, mean HbA1C decreased from 8.2 to 6.2% (24.4 %; $p < 0.05$). The same table also showed that glibenclamide significantly increases HDL (42.4±3.6; 48.9 ± 4.3 mg/dl ; ($p < 0.05$) and TG levels (145.6 ± 7.5 ; 157.7 ± 8.3; $p < 0.05$) after 14 weeks of treatment. The insignificant effect was observed with glibenclamide therapy in serum total cholesterol and LDL concentrations.

Table 1. In vivo effect of glibenclamide on laboratory findings.

Test	Control	SD	Pre-treatment	SD	Post-treatment	SD	P value
Glucose (mg/dl)	88.3	13.6	175.6	10.1	129.5	9.5	< 0.05
HbA1c (%)	4.5	0.8	8.2	1.1	6.2	0.5	< 0.05
T. Chol. (mg/dl)	143.2	11.4	151.3	11.4	154.7	8.5	NS
TG (mg/dl)	123.1	12.2	145.6	7.5	157.7	8.3	< 0.05
LDL (mg/dl)	68.3	6.8	72.3	3.4	68.9	5.7	NS
HDL (mg/dl)	47.7	7.8	42.4	3.6	48.9	4.3	< 0.05

HbA1c = glycosylated hemoglobin.Total cholesterol (T.Chol.), Triglyceride (TG), light density lipoprotein (LDL), heavy density lipoprotein (HDL).

Significant ($p < 0.05$) , NS = non-significant.

Discussion:-

The traditional procedure to control the diabetes is by using one antidiabetic agent or combination of agents. Effective blood glucose control is the key for preventing or reversing diabetic complications and improving the quality of life in patients with diabetes. Diabetic patients usually suffer from dyslipidemia which includes elevated levels of LDL and triglyceride. Level of HDL is known as risk factor for cardiovascular disease, Thus a sustained

reduction in hyperglycemia will decrease the risk of developing microvascular complications (Skrapari et al. 2001).This study was conducted to validate the effect of glibenclamide on fasting blood sugar,HbA1c and lipid profile in Type 2 diabetics. Glibenclamide showed significant reduction in fasting blood glucose after 14 weeks of treatment. This is in agreement with the result of Reyadh (2012)and Rosak et al. (2002). Glibenclamide has the mechanism of action in lowering blood glucose like Sulfonylureas which acts by stimulating the release of insulin from the B-cell of the pancreas through inhibiting ATP-sensitive K channels, thereby activating the Ca^{++} channel with increase in intracellular calcium to release insulin (Frances. 2005).The parameter used to assess the efficacy of drug therapy along with fasting glucose level was the glycosylated haemoglobin HbA1c which was improved as shown in this study after 14 weeks of treatment with glibenclamide. This finding was similar to study by Duckworth et al. (2003) and Meenu et al. (2014). The present study showed that treatment with glibenclamide resulted in increased HDL level as reported by Santana et al. (2004) and supported by YKi-Jarvinen (2004). It is widely known that there is an inverse relation between the level of HDL and the cardiovascular risk(Schaefer et al 2014). In this study glibenclamide causes a significant elevation in HDL that will reduce the risk of cardiovascular diseases. It was observed a non- significant reduction in low density lipoprotein in diabetic patients enrolled in the present study, which was in agreement with Tamai et al. (1982). Despite TG level was significantly elevated compared with the level in pretreated patients , it is still within the normal range which contrast the results obtained by Mori et al. (2006) and Skrapariet al.(2001) in which glibenclamide produced a significant decrease in TG level. This such contradictory result may be attributed to type of life style including the diet habit.

Conclusion:-

The use ofglibenclamide for 14 weeks in the treatment of diabetes of type 2 provides better protection against cardiovascular complications of DM and hence better prevention of complications like atherosclerosis.

References:-

1. Carl, A., David, E. (2014). Tietz Fundamentals of clinical chemistry. 7th edition.. Pub. Saunders, USA.
2. Duckworth, W., Marcelli, M., Padden, M., et al. (2003). Improvements in glycemic control in type 2 diabetes patients switched from sulfonylurea coadministered with metformin to glyburide-metformin tablets. J Manag Care Pharm. 9(3): 256-62.
3. Frances , M. (2005). ATP-sensitive potassium channelopathies: focus on insulin secretion. J Clin Invest. 115(8): 2047–2058.
4. . Hong, L., Richard, M. (2013). Determination of Percent Hemoglobin A1c Using a Potentiometric Method. Anal. Chem. 85 (3), 1834–1839
5. Katzung, B. (2001). Basic and Clinical Pharmacology, 8th edition, Lange/ McGraw Hill Publishers. 725.
6. Manjusha, H., Sriparna K, Sanjib B, Pallab K, Malaya G, Upal K. (2011). Evaluation of hypoglycemic and antihyperglycemic effects of Luffacylindrica fruit extract in rats. Journal of Advanced Pharmacy Education & Research. 2: 138-146.
7. Meenu, R., Shailesh, Y., Parveen, G. et al. (2014). A study comparing the effect of Glimepiride and Glibenclamide on Glycosylated Hemoglobin (HbA1c) in Type II Diabetes Mellitus patients. International Journal of Medical Science and Public Health. 3 (1): 35 – 37
8. Mori, Y., Itoh, Y., Obata, T., Tajima, N. (2006).Effect of pioglitazone vsglibenclamide on postprandial increase in glucose and triglyceride levels and on oxidative stress in Japanese patients with type 2.Endocrine. 29(1):143-8.
9. Omonkhelin, J., Eric, K. (2011) .Co-administration of Glibenclamide and Amlodipine Induces Resistance to Hyperglycemic Treatment in Streptozotocin Induced Adapted/Non adapted Diabetic Rats. Clin. Exp.Pharmacol. 1:12 – 7.
10. Pravinkumar, R., Talele, G. (2012). Adverse effects of metformin in combination with glimepiride and glibenclamide in patients with type 2 diabetes mellitus. Asian Journal of Pharmaceutical and Clinical Research. 5(1): 108 – 110
11. Rosak. C., Haupt, E., Walter, T. et al. (2002). The effect of combination treatment with acarbose and glibenclamide on postprandial glucose and insulin profiles: Additive blood glucose lowering effect and decreased gypoglycaemia. Diabetnutrmetab.15: 143-151.
12. Reyadh H. (2012). Effects of Metformin, Glyburide and their Combination on Lipid Profile in NIDDM Patients. Medical Journal of Babylon. 9 (4). 936 – 945.
13. Santana, L., de Sa, M., Ferriani, R.et al. (2004). Effect of metformin on the clinical and metabolic assessment of women with polycystic ovarysyndrome. Gynecol. Endocrinol. 19:86-96.

14. Schaefer, E., Anthanont, P., Asztalos, B. (2014). High-density lipoprotein metabolism, composition, function, and deficiency. Curr. Opin.Lipidol. 25: 194–99.

15. Skrapari, I., Perrea, D., Ioannidis. et al. (2001). Glibenclamide improves postprandial hypertriglyceridaemia in type 2 diabetic patients by reducing chylomicrons but not the very low-density lipoprotein subfraction levels. Diabet Med.18(10):781-5.

16. Sona, V., Augusti, T., Varghese ,C., Regi, J (2009);. Effect of insulin, glimepiride and combination therapy of insulin and metformin on blood sugar and lipid profile of NIDDM patients.Indian Journal of Clinical Biochemistry. 24 (2) 175-178.

17. Tamai, T., Nakai, T., Yarnada, S. et al. (1982). The effect of Glibenclamide and insulin on plasma high density lipoprotein in diabetes. Artery. ; 9:477-93.

18. Vitthal, S., Kalekar, M., Samant, B., Chaudhari, D., Vijay, P., Rasika, D (2014).. To Compare the Effect of Oral Hypoglycaemic Drugs Glibenclamide and Pioglitazone on Blood Sugar, Lipid Abnormalities in Type 2 Diabetes Mellitus. International Journal of Health Sciences and Research. 4 (4) ; 53 – 60.

19. Waller, D., and Renwick, A. (1994). Principles of medical pharmacology. London. Bailiere tidal pub. 246 – 249.

20. YKi-Jarvinen, H. (2004). Thiazolidinediones. N Engl J Med. 351: 1106-18.