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EVALUATION OF ROLE OF ORAL ANTI-DIABETIC DRUGS ON LIPID PROFILE IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

Diabetes mellitus is a group of metabolic disorder characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative insulin deficiency. The present study was carried out to establish a correlationship between hyperglycemia of varying intensity with hyperlipidemia in NIDDM patients taking oral hypoglycemic drugs. The objective of the work was to find out whether hyperlipidemia was affected due to administration of a particular group of hypoglycemic drug. The total numbers of patients under study were 36 and control group consisted of 15 persons. All the 36 cases were divided according to age groups, sex, socio-economic status and dietary habits. Patients were divided into three groups i) patients taking Sulfonylurea ii) patients taking Biguanides and iii) patients taking Thiazolidinedione group of oral hypoglycemic. A morning blood sample after overnight fast was collected and serum total cholesterol, HDL and LDL cholesterol, triglycerides and plasma glucose were estimated. From the present study it is clear that Biguanides are more effective than Sulphonylureas in improving lipid profile in NIDDM cases. Also, the study suggests that NIDDM patients on oral hypoglycemic drugs are not susceptible to develop coronary artery disease.

KEY WORDS

sulphonylureas,biguanides,thiazolidinedione

INTRODUCTION

Diabetes mellitus is known to human being since more than 2000 years. The earliest description was by the ancient Hindu Physician in Charaka Samhita as MADHUMEHA 3000 B.C. Susruta about 400 B.C described the diabetic Syndrome as characterised by a honeyed Urine (Madhumeh). Susruta also described and mentioned two varieties of Madhumeh of which one group of Patients were lean and thin and there was wasting leading to death. There was another variety of Patients who were obese with complication and died a slow death(1,2,3).

Diabetes mellitus is a group of metabolic disorder characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative insulin deficiency. Diabetes mellitus is of two types –Type 1 and Type 2 diabetes mellitus.
Type 2 diabetes characterized by target tissue resistance to Insulin is epidemic in industrialized societies and is strongly associated with obesity, however the mechanism by which increased adiposity causes insulin resistance is unclear.
Steppan C M et al (1) showed that Adipocytes secrete a unique signalling molecule which they have named Resistin for resistance to Insulin. Circulating Resistin levels are decreased by the anti-diabetic drug Rosiglitazone and increased in diet induced and genetic forms of obesity. They also observed that Insulin stimulated glucose uptake by adipocytes is enhanced by neutralization of Resistin and is reduced by Resistin treatment(4,5,6,7,8,9).
Metabolic syndrome X includes glucose intolerance or type 2 diabetes, dyslipidemia and arterial hypertension which are classical cardiovascular risk factors. Insulin resistance is the cornerstone of Metabolic Syndrome X, with secondary hyperinsulinism. Upper body obesity is associated with metabolic syndrome X. According to Daubresse JC(2), Diet is the first step in treating these patients and reducing caloric intake is necessary in most of them. He suggested Polyunsaturated and monounsaturated fats in place of Saturated fat, also long chain carbohydrates with low glycemic index and regular physical activity. If these life style modifications fail, Drugs like Biguanide and glitazone are good(10,11,12,13,14,15,16,17,18,19).
The present study was carried out to establish a correlation between hyperglycemia of varying intensity with hyperlipidemia in NIDDM patients taking oral hypoglycemic drugs.
The objective of the work was to find out whether hyperlipidemia was affected due to administration of a particular group of hypoglycemic drug.

MATERIALS AND METHODS

The present work has been conducted in the Department of Biochemistry, Patna Medical College, Patna. The Cases studied were selected at random from Patna Medical College and Hospital, Patna, Outdoor, Indoor wards of Medicine Department and also from Diabetic clinic of PMCH. Cases were on Oral hypoglycaemic drugs for atleast 1 month duration and they were asked to remain empty stomach on the day of Sample Collection after overnight fasting.
The total number of Cases in study were 36 and Normal persons were 15.

Different groups in Study are :-
(1) Normal Persons not having any apparent disease.
(2) Patients taking Oral hypoglycemic drugs for atleast last 1 month.
(ii) Sulfonylureas (ii) Biguanides
(iii) Thiazolidinediones.
Cases were followed at 3 wks interval upto 6 weeks of oral hypoglycemic therapy after first reporting. Age group of all the persons were between 32 Yrs to 77 Yrs
The following tests were done in each Sample during the Study.
(1) Serum total Cholesterol
(2) Serum HDL&LDL Cholesterol
(3) Serum Triglyceride
(4) Plasma glucose - Fasting
- 2½ hrs after 75 gm glucose
Selection of Cases :- Only those persons were included in the present study, who had no other existing diseases, which were known to influence lipid metabolism and thereby affecting the lipid profile. Disease like jaundice, Renal disease, Hypertension, thyroid were discarded. A list of questions were asked as given in the case sheet proforma.

Collection of Blood Sample **:-** A morning sample of venous blood after overnightfast was collected in a dry and sterile syringe. First arm was extended and a rubber tourniquet applied

a few inches above the elbow. Skin over the antecubital vein were cleaned by rubbing with spirit. A well sharp sterile hypodermic needle fixed on to a syringe of 5ml capacity was inserted into vein and Plunger was withdrawn slightly. As soon as blood appears Tourniquet was released and 5ml of blood was withdrawn into the Syringe. A small cotton swab soaked in spirit was placed at the Needle insertion site and needle withdrawn. Cotton swab held firmly for few minute until bleeding stopped. Needle removed from the Syringe. 3 ml of blood transferred to Plain sterile vial and 2 ml of blood transferred to Sodium Fluoride Containing vial. Blood in Plain sterile vial was kept inclined to allow to clot. When Blood clotted, Vial was kept vertical for some time. Clot shrinks and serum separated. This serum was centrifuged at 3000 r.p.m for 5 minutes to separate RBC from Serum. Clear Supernatant Serum was pipetted out and was used for various Serum lipid profile estimation.

Sodium fluoride containing Blood was centrifuged at 3000 rpm for 5 min to separate red cells from clear supernatant Plasma. Supernatant Plasma was pipetted out and used for sugar estimation in Plasma.

Patient was then given 75 gm glucose orally in 200 ml water and another blood sample of 2 ml was taken 2½ hrs after meal. Plasma was separated by centrifugation in a similar way and postprandial sugar in plasma was estimated.

Method of Serum Triglyceride estimation

Merck's Kit used for estimation of Serum Triglyceride level. It is based on GPO-POD method, an enzymatic method.

Principle :- Triglyceride is hydrolysed to Glycerol and Free fatty acid by Lipoprotein lipase. In the presence of ATP and Glycerokinase (GK) the glycerol is Converted to Glycerol -3. Phosphate and ADP. Glycerol-3-Phosphate is then oxidised by Glycerol 3 Phosphate oxidase (GPO) to yield Hydrogen peroxide and Dihydroxyacetone phosphate in presence of O_2 .

Hydrogen peroxide in presence of peroxidase (POD) enzyme react with chromogen (4 Chlorphenol +4 aminoantipyrine) to form coloured complex (chinonimine). The intensity of colour developed is proportional to the triglyceride concentration which is measured in a Photocolorimeter with green filter 520 nm.

Method for Total Cholesterol estimation.

For total cholesterol estimation, Accurex kit was used. It is based on enzymatic method.

Principle :- Cholesterol esterase (CHE) hydrolyses cholesterol esters into free cholesterol and fatty acids. Free cholesterol is oxidised by the cholesterol oxidase (CHO) to Cholest-4-en-3-one and hydrogen peroxide (H_2O_2). This hydrogen peroxide in presence of peroxidase (POD)couples with 4-aminoantipyrine and phenol to produce red coloured quinoneimine dye. The intensity of colour produced is proportional to the cholesterol concentration.

Method for HDL Cholesterol estimation

CREST Biosystems Kit used for estimation of Serum High density lipoprotein cholesterol. It is based on PEG Precipitation Method.

Principle :- Very low density lipoprotein (VLDL) and Low density lipoprotein (LDL) of Serum precipitates out when Serum reacts with polyethylene glycol contained in the Precipitating reagent. High density lipoprotein (HDL) remains in the Supernatant fluid which is then determined by using working cholesterol reagent.

Determination of Serum LDL cholesterol and VLDL cholesterol

In absence of a separate estimation of LDL and VLDL cholesterol indirect method has 0 been used in accordance with the outline of Freidewald's Formula. (Freidewald W.T. et al 1972).

Here VLDL cholesterol can be indirectly ascertained as $1/5^{th}$ of the triglyceride value

The LDL cholesterol has been Calculated from the estimated values of triglyceride, Total cholesterol, HDL cholesterol which were directly measured in serum by enzymatic method as described above.

The value of LDL cholesterol is calculated as

LDL cholesterol (mg/dl)
= Total cholesterol (mg/dl) – HDL cholesterol (mg/dl)
$$- \frac{\text{Triglyceride}}{5} \text{ (mg/dl)}$$

Estimation of Blood Sugar by O – Toluidine method

Principle :- Glucose condenses with O – toluidine in glacial acetic acid when heated at 100˚c. The product formed is a blue green N – glucosylamine, the colour so produced is proportional to the amount of glucose concentration which is measured at 630 nm (redfilter

RESULTS

Table No.1
Treatment wise table of All drug groups

Group of Drug	*No. of Patients*	*%*
SU	28	77.78
BI	7	19.44
TH	1	2.78
Total	36	100

Table No. 2
Comparison of Mean plasma sugar in fasting and 2½ hrs after meal for patients treated with drug group SU and BI.

Drug group SU						*Drug group BI*				
Group			*N*	*Mean (mg%)*	*SD*	*N*	*Mean (mg%)*	*SD*	*t value*	*p value*
Study group	A	F	28	105.07	54.84	7	108.43	38.36	0.188	> 0.10
		PP	28	149.60	76.34	7	161.86	45.88	0.543	> 0.10
	B	F	18	79.72	9.05	7	79.86	4.81	0.05	> 0.10
		PP	18	110.94	17.14	7	111.43	7.09	0.1010	> 0.10
	C	F	3	77.67	4.93	3	78	2	0.107	> 0.05
		PP	3	104.67	3.78	3	104.67	3.21	0	> 0.10

F = fasting, PP = 2½ hrs after meal

Table No. 3

Comparison of Mean Triglyceride level (mg%) for patients treated with SU and BI group of drugs.

Drug group SU					Drug group BI				
Group		*N*	*Mean (mg%)*	*SD*	*N*	*Mean (mg%)*	*SD*	*t value*	*p value*
Control		15	121.60	27.21	15	121.60	27.21		
Study	A	28	161.07	79.87	7	157.71	42.97	.1067	> 0.05
	B	18	141.44	54.24	7	140.28	30.50	.0529	> 0.05
	C	3	130.33	32.52	3	130	8	.0170	> 0.05

Table No. 4

Comparison between Mean Serum Triglyceride level of SU and BI drug group taking patients in different Age groups.

SU						*BI*				
Age group (yrs)	*N*	*Mean*	*SD*	*t value*	*P value*	*N*	*Mean*	*SD*	*t value*	*P value*
31- 50	18	156.11	81.16			2	170	42.43		
51- 80	10	170	80.98	0.4346	> 0.10	5	152. .8	47.06	0.4693	> 0.10

DISCUSSION

In the present study three groups of patients were studied. Each group of patients were on one type of oral hypoglycemic drugs (e.g. – Sulfonylurea Biguanides or Thiazolidinediones). Total number of patients taking sulfonylurea group drug in the study was 28 which is 77.78% of total study group. The total number of patients taking Biguanide group drug was 7 which is 19.44% of total and the total number of Thiazolidinedione group drug was only 1, which is 2.78% of total (Table No. 5).

Table No. 5

Comparison of Mean Total cholesterol for patients treated with SU and BI drugs.

Drug group SU					*Drug group BI*				
Group		*N*	*Mean (mg%)*	*SD*	*N*	*Mean (mg%)*	*SD*	*t value*	*p value*
Control		15	158.33	31.19	15	158.33	21.19		
Study	A	28	174.54	40.98	7	166.57	33.03	0.4755	> 0.05
	B	18	164.33	34.61	7	154.86	23.85	0.6613	> 0.05
	C	3	142	30.12	3	141.67	20.21	0.0158	> 0.05

All these patients were on oral hypoglycemic drugs for at least 1 month duration and was followed at 3 different intervals as shown in Table (6,7, 10, 13, 16) for lipid profile.

Table No. 6

Comparison between Mean total cholesterol level in different Age groups in SU & BI drug group taking patients.

SU						*BI*				
Age group (yrs)	*N*	*Mean*	*SD*	*t value*	*p value*	*N*	*Mean*	*SD*	*t value*	*P value*
31-50	18	169.11	44.12			2	157	1.42		
51-80	10	185.3	33.69	1.0873	> 0.10	5	170.4	39.66	0.7545	> 0.10

Table No. 7

Comparison between Mean HDL cholesterol for patients treated with SU and B I group of Drugs.

Drug group SU					*Drug group BI*				
Group		*N*	*Mean (mg%)*	*SD*	*N*	*Mean (mg%)*	*SD*	*t value*	*p value*
Control		15	52.27	6.11	15	52.27	6.11		
Study	A	28	47.93	9.96	7	44	7.66	0.970	> 0.05
	B	18	49.11	7.26	7	47.28	8.98	0.530	> 0.05
	C	3	52.33	2.08	3	51	6.08	0.358	> 0.05

Table No.8

Comparison of Mean LDL cholesterol for patients treated with SU and BI drugs in mg%.

Drug group SU					*Drug group BI*				
Group		*N*	*Mean*	*SD*	*N*	*Mean*	*SD*	*t value*	*p value*
Control		15	81.8	20.77	15	81.8	20.7		
Study	A	28	95.64	38.02	7	91.14	37.55	0.2807	> 0.05
	B	18	87.33	32.78	7	79.57	30.25	0.5418	> 0.05
	C	3	63.6	30.33	3	61.33	20.03	0.1082	> 0.05

Effect on Plasma Glucose after Antidiabetic therapy Among BI group drug taking patients Mean fasting plasma glucose at the time of reporting, at 3 wks and after 6 weeks of reporting were 108.43, 79.86. and 78 mg% respectively. Mean post prandial plasma glucose at above intervals were 161.86, 111.43 and 104.67 mg% in BI group drug taking patients.

This study explains that fasting and post prandial mean plasma glucose lowers with duration of treatment and comes down to near about mean plasma glucose level of control group in both drug group taking patients. From the comparative study of plasma glucose in both drug groups taking patients, it is clear that mean plasma glucose (F and PP) level in sulfonylurea group drug taking patients is lower than the mean plasma glucose level (F & PP) in biguanide group drug taking patients at the time of reporting and at 3 weeks of reporting. This could be due to poor control of hyperglycemia. When p-value was estimated to analyse this difference, it is found statistically not significant. Mean plasma glucose level at 6 weeks of reporting is equal in both sulfonylurea and Biguanide group drug taking patients. This explains that both oral hypoglycemic drugs (Sulfonylureas and Biguanides) are equally effective in lowering plasma glucose in NIDDM cases.

It has been well documented that the mechanism of action of sulfonylurea group drug is to stimulate insulin release from pancreatic β-cells. Mechanism of action of Metformin is unclear but particularly effective in reducing hepatic gluconeogenesis by interfering with lactate oxidation and uptake by the liver. It also slows down the gastrointestinal absorption of glucose etc.

Effect of Oral antidiabetic therapies on serum Triglyceride level

Statistical analysis of Table (7) was done to see the effect of sulfonylurea and Biguanide group drugs on mean serum Triglyceride level. Mean TG level in NIDDM patients on sulfonylurea group of drug at the time of reporting, at 3 weeks and 6 weeks of reporting are 161.07, 141.44 and 130.33 mg% and in those taking Biguanide group of drug are 157.71 mg%, 140.28 mg% and 130 mg% respectively at above mentioned intervals. These findings show that Mean TG level in sulfonylurea group taking patients is higher than the Mean TG level in Biguanide group taking patients during the whole follow up period. This difference in Man TG level could be due to better control by Biguanide group drugs than sulfonylurea group drug. But when t value calculated and p value derived then it was found that this difference is not statistically significant. From the present study it is also concluded that Mean Triglyceride level decreases with duration of treatment in both groups (Sulfonylurea and Biguanide group

drug taking patients) and comes to near about normal level but not below normal TG level.

There are several metabolic factors in NIDDM, that predisposes to hypertriglyceridemia. Most notably it may be due to increased recycling of free fatty acids from peripheral tissues to liver, where they provide a substrate for hepatic triglyceride synthesis. Secondly the impaired activity of lipoprotein lipase, the principal peripheral enzyme involved in the clearance of plasma triglyceride from the capillary circulation into the muscle, heart and kidney etc. The activity of this enzyme can be reduced upto 40% in some untreated or uncontrolled NIDDM patients (Taylor KG, Goltan DG, Holdswarth G et al 1979)(19,20,21,22,23).

This study also suggests that as treatment duration increases Mean TG level comes down towards normal level but remains above the mean TG level in control group. This difference in Mean TG level could be due to poor control of hyperglycemia. But when t value and p value was calculated, it was found that this difference is statistically not significant.

The role of Triglyceride as a cardiovascular risk factor in Non-diabetic population is debatable. Population studies of diabetes consistently and strongly suggest that hypertriglyceridemia is a significant risk factor for coronary heart disease (West KM, Ahuja Benett ph et al. 1983). e.g. – in the WHO's Cross sectional multinational study of more than 1900 persons with NIDDM cases, plasma triglyceride levels were significantly related to coronary heart disease, independent of other risk factors. Hypertriglyceridemia is related in part to the degree of diabetic control (Eckel RH, Mclean EB et al. 1981)(24,25,26,27,28,29,30).

Paris prospective study has suggested TG as an important risk factor. Elevated plasma level of tissue plasminogen activator inhibitor associated with hypertriglyceridemia has been suggested as the possible mechanism in the genesis of coronary artery disease. The TG levels considered normal in Caucasian population may be high for the Indian population. According to Enas A, Mehta J et al 1995, Mean TG level of Indians with coronary heart disease are 20-40 mg/dl lower than in Caucasian with coronary heart disease.

In the present study the serum TG levels in males and females were analysed with the study group taking sulfonylurea (Table No. 9) and it was found that although Mean TG in Male is more than that of female but this difference is not significant statistically.

Table No. –9

Comparison between Mean Serum HDL cholesterol level in SU group taking patients in different Sexes.

SU					
Sex	*N*	*Mean*	*SD*	*t value*	*P value*
Male	20	48.15	10.16		
Female	8	47.38	10.098	0.1820	>0.10

A comparison has been done between two age groups 31-50 yrs and 51-80 yrs in respect of Mean serum triglyceride level in both types of study group (Table 8). It is seen that Mean TG level in sulfonylurea group drug taking patients in 31-50 yrs age group is 156.11 mg% and that in 51-80 yrs age group is 170 mg% with p value > 0.10 i.e. this difference in Mean TG is not significant. Similar finding found in Biguanide taking study group in which Mean TG among 31-50 yrs age group is 170 mg% and that among 51-80 yrs age group is 152.8 mg% with P value > 0.10 i.e. statistically not significant. This shows that serum triglyceride level increases as Age advances.

Table No. 10
Comparison between Mean HDL cholesterol level in SU and BI taking patients in different Age groups.

SU						*BI*				
Age group yrs	*N*	*Mean*	*SD*	*t value*	*p value*	*N*	*Mean*	*SD*	*t value*	*p value*
31- 50	18	47.44	10.93			2	46	11.31		
51- 80	10	48.8	8.42	0.3676	> 0.10	5	43.2	7.29	0.3240	> 0.10

Effect of Oral hypoglycemic therapy on serum Total Cholesterol

Mean total cholesterol level at the time of reporting is significantly higher than that of control group. The reason behind this may be due to :

(i) Longer duration of disease due to late diagnosis because people of this region are not very much health conscious.
(ii) Inadequate physical exercise.
(iii) Anxiety and smoking.

The basic mechanism may be due to Hyperinsulinemia which is particularly very common in patients with NIDDM who are on oral hypoglycemic therapy. Hyperinsulinemia also may play a role in promoting atherosclerosis by causing proliferation of smooth muscle and synthesis of cholesterol as well as by increasing level of growth hormone (Stout RW, Insulin and Atheroma, an update, 1987).

According to Berharld H et al 1965 in his long term observation of oral hypoglycemic agents in type 2 DM, about 15-20% of patients have little or no glycemic response to sulfonylurea (Primary failure), approximately 50% will achieve acceptable or normal glucose level and remainder will achieve between acceptable and poor glycemic control. The increased cholesterol level in NIDDM patients may be due to primary failure or poor glycemic control because these factors lead to massive triglyceridemia associated with Hypercholesterolemia. This condition is also called diabetic lipemia. (Current topic in diabetic research page no. 124 editor F. Belfiore, Marja Rilta et al 1993). However, to find out whether a patient is fully under control it would have been better to estimate glycated haemoglobin. To find out whether the hyperlipidemia is mainly due to uncontrolled diabetes, further study would be required with an aim to observe the glycosylated haemoglobin in all such diabetic cases.

A comparison has been done between two age groups 31-50 yrs and 51-80 ys in respect of serum total cholesterol level in both study groups taking sulfonylurea and Biguanide separately (table 11). In the present study Mean total cholesterol in sulfonylurea group drug taking patient in Age groups 31-50 yrs and 51-80 ys are 169.11 mg% and 185.3 mg% respectively. Mean serum total cholesterol level in Biguanide group drug taking patients in age groups 31-50 yrs and 51-80 yrs are 157 mg% and 170.4mg%. In both study groups it has been seen that mean serum total cholesterol level is more in Age group 51-80 yrs than that in 31-50 yrs.

This could be due to inadequate exercise, sedentary habits, Anxiety etc. But when t value and p value estimated, it is found that this difference is not significant statistically (P > 0.10).

A comparative study was done between different sexes in the study group receiving sulfonylurea group drug (Table No. 12). In the present study Mean total cholesterol level in Male and Female in patients taking sulfonylurea therapy are 171.15 mg% and 184.25mg% respectively. This finding reveals that mean total cholesterol level is significantly higher in case of Female than that of Male. The

reason could be due to sedentary habits in female and altered dietary habit, more outdoor activity in males, anxiety etc.
The effect of lowering cholesterol level by physical exercise has been documented by many workers (Carlson et al 1964, Good et al 1966, Froberg et al 1971, Levis et al 1976)(31,32,33,34,35,36).
But when t value and p value were estimated for sex wise difference in mean total cholesterol, it was found that this difference is statistically not significant (P > 0.10).

Effect of oral antidiabetic therapies on serum HDL Cholesterol

When the Mean HDL cholesterol level in Sulfonylurea group drug taking patients and Biguanide group drug taking patients are compared, it is found that Mean HDL cholesterol level in Biguanide group drug taking patients is less than that in sulfonylurea group drug taking patients. But the difference in Mean HDL cholesterol level between the two groups is not statistically significant (p>0.05). Although these values are normal for Western literature but this value is a risk factor for Atherosclerosis in Indian subcontinent. This was observed also in work done by Krishna Swami, Prasad NK, Jose JA et al 1989, who suggested that weight loss and increased physical activity improves the lipid profile by increasing HDL cholesterol which is protective for cardiovascular complication.
Several literatures are available which clearly indicate that Indian population are physically more active and do hard wok compared to Western who are mainly confined to mental work. (American Family Physician Personal Communication 2000).
This table also reveals that mean HDL cholesterol level in NIDDM patients on oral hypoglycemic therapy at 3 weeks and 6 weeks of reporting are more than that at the time of reporting which reveals that as Hyperglycemia improves the mean HDL cholesterol level also improves.
A comparison has been done between Mean HDL cholesterol level in Age group 31-50 years and that in 51-80 yrs Age groups (Table No. 14). Mean HDL in Age group 31-50 yrs is 47.44 mg% and in Age group 51-80 yrs is 48.8mg% among NIDDM cases on sulfonylurea group drug. This shows that HDL cholesterol level in 31-50 yrs age group is less than that in Age group 51-80 yrs. But the difference is not statistically significant. Mean HDL cholesterol level in Age groups 31-50 yrs and 51-80 yrs are 46 mg% and 43.2 mg% respectively among NIDDM patients on Biguanide group drug therapy. This shows that Mean HDL levels is lower in age group 51-80 yrs than that in age group 31-50 yrs. This difference could be due to better effectiveness of Biguanide group drug in middle age group. when t value and p-value was calculated this difference is not significant statistically (P > 0.10).

Effect on Serum LDL Cholesterol

This also shows that Mean LDL cholesterol level in control group is 81.8 mg%. Mean LDL level is higher in NIDDM patients on hypoglycemic drug therapy than the control group at the time of reporting and at 3 weeks of reporting. This difference could be due to poor control of diabetes, westernised dietary pattern and also due to alteration in LDL cholesterol metabolism. When t-value and p-value estimated it is found that this difference is not significant (p>0.05). Mean LDL cholesterol level at the time of reporting, at 3 weeks and 6 weeks of reporting in both drug groups reveals that with control of hyperglycemia by oral hypoglycemic drugs LDL level is also lowered.

A comparison done for sex difference in respect of Mean LDL cholesterol level in NIDDM patients on sulfonylurea drugs (Table No. 18). Mean LDL cholesterol level in Male is 88.3 mg% and in Female is 114 mg%. This shows that Mean LDL cholesterol level is less in Male than that in female NIDDM patients. This difference could be due to increased physical activity by male. When t value and p-value calculated this difference is not significant statistically (p>0.10).
Overall lipid profile of Normal person and NIDDM patients on oral hypoglycemic therapy:

From above discussion it is apparent that in Normal individuals (control group) the lipid status with respect to Triglyceride is normal with a Range, Mean and SD of 80-180 mg%, 121.60 mg% and 27.21 mg% respectively; with respect to serum total cholesterol is normal with a Range, Mean and SD of 137-225 mg%, 158.33 mg% and 21.19 respectively; with respect to HDL cholesterol, is normal with a Range, Mean and SD of 39-67 mg%, 52.27mg% and 6.11 respectively and with respect to serum LDL cholesterol is normal with a range, Mean and SD of 59-139 mg%, 81.8mg% and 20.77 respectively.

It was seen from the study that Mean triglyceride level in NIDDM cases on SU and BI group drugs at the time of reporting were 161.07 mg% and 157.71mg% which lowered down to 141.44mg% and 140.28mg% after 3 weeks of reporting and to 130.33 mg% and 130 mg% after 6 weeks of reporting respectively which is similar to the finding of Krishna Swami, Prasad NK et al who in 1989 suggested that triglyceride level upto 150 mg% is desirable range for Asian population but TG levels in between 150-170mg% is borderline risk group and 170 mg% is high risk group for developing cardiovascular complications. Also most of the studies related to diabetes in Asian region believe that TG level upto 150 mg/dl is normal (Indian Personal Communication, 2000).

Both of above study group lipid profile suggests that controlling hyperglycemia by oral hypoglycemic drugs also improves the various lipid profile which is in accordance with the finding of Hsueh WA, Law RE et al who studied and found that Metformin lowers LDL cholesterol and triglycerides while troglitazone reverses many of the components associated with Insulin resistance syndrome.

According to Upendra Kaul et al National Cholesterol Eradication programme guidelines may be too liberal in Indian context, Framingham data suggests a markedly attenuated risk below a total cholesterol of 160 mg%. The optimal level of total cholesterol for primary prevention should be below 200 mg/dl and for secondary prevention below 150 mg/dl. In Asian Indians the desired Triglyceride level should be < 150 mg/dl and total cholesterol/HDL-ratio should be below 4.5 (Enas A, Mehta SL, 1995).

It is seen in both the study that HDL level increases with duration of Hypoglycemic therapy which is similar to the finding by Dunn FL et al who reported that acute effects of sulfonylurea are principally mediated by increase in pancreatic secretion of Insulin. When sulfonylurea therapy is effective in lowering glucose levels, the accompanying elevated lipid levels are significantly reduced as well.

It is also seen from the result table that HDL level increases with duration of oral hypoglycemic therapy. This findings is similar to that of Melander A et al observation who demonstrated that glycemic control improvement is usually accompanied by decrease in plasma level of Triglycerides, VLDL and apolipoprotein B. With improved glycemic control HDL cholesterol sometimes also increases moderately but not normalized completely even when other lipids are brought within the normal range.

De Fronzo RA et al also suggested that Metformin reduces Insulin resistance as well as improves lipid profile slightly(37,38,39,40).

Brunova J et al recorded in his study of 40 middle aged diabetics and reported that there was reduced HDL cholesterol, elevated Triglycerides and total cholesterol levels. After control of diabetes the cholesterol and triglyceride levels became normal, the HDL cholesterol levels remained however low. This low level of HDL indicate the increased risk of Atherosclerosis.

To conclude, both the oral anti-diabetic drugs (SU and BI) improves the lipid profile with slightly better improvement with Biguanide therapy.

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