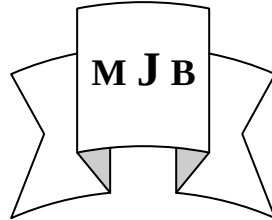


## Study Effect of Glimepiride and Repaglinide on CIMT and Long Glycemic Control in Type 2 Diabetic Patients Double Blind Study

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**Received 4 February 2013**

**Accepted 15 April 2013**

### **Abstract**

**Background** Diabetes mellitus (DM) is one of the main risk factors for cardiovascular complications ,namely coronary ischemia, Peripheral vascular disease, and stroke. Atherosclerosis is highly associated with Diabetes mellitus . Carotid intima media thickness (CIMT) is used extensively as a method to detect atherosclerosis.

**Aim of the study** repaglinide and glimepiride are newly introduced and used for non-insulin-dependent diabetes mellitus (NIDDM) ,the study aim to compare the difference in their effect on CIMT.

**Patients and Methods** The study enrolled 62 patients NIDDM all from Al Hakeem Diabetic center in Najaf in period from January 2011 to the March 2012 all had their recording files with mean age ( $53 \pm 0.23$ ), 35 females and 27 males with body mass index (BMI) Mean(  $28 \pm 0.4$  ) divided into two groups (blindly grouped) each one 31 used Repaglinide 3mg/day and second one used Glimepiride 3mg/day. followed after 6 months and then after 12 months record the hemoglobin A<sub>1c</sub>(HbA<sub>1c</sub>), lipid profile , CRP, blood pressure ,the blood urea and serum Creatinine and studying the CIMT of both internal carotid and the common carotid arteries using ultrasonic Doppler study .

**Results** There was a significant(  $p < 0.05$ ) reduction in CIMT of left internal carotid and the right common carotid arteries in patients treated with repaglinide compares to those patients treated with glimepiride and there was also reduction in the other parameters Low-density lipoprotein (LDL) , Triglyceride (TG) ,HbA<sub>1c</sub> still these decrement were not a significant one.

**Conclusion and recommendation** repaglinide is better in reduction of the CIMT than Glimepiride in spite of insignificant reduction in the lipid profile or HbA<sub>1c</sub>. We recommend to study what dose required to achieve a best reduction in CIMT.

**Key Words** : diabetes ,glimepiride, repaglinide, CIMT.

### **الخلاصة**

دراسة مزدوجة غير محددة لتأثير عقار ريباغليدين وعقار رابكليدين على ثخن الطبقة المبطنية الداخلية للشرايين العنقية في النوع الثاني لمرض السكري مرض السكر يشكل احد اخطر عوامل مضاعفات امراض جهاز الدوران و الأوعية الدموية وبالأخص عدم كفاءة الشرايين القلبية وامراض الأوعية الدموية للأطراف والجلطة الدماغية إن تصلب الشرايين يتصاحب مع مرض داء السكر وان قياس ثخن الطبقة المبطنية الداخلية للشرايين العنقية يستخدم بشكل واسع للتعرف على تصلب الشرايين-تهدف الدراسة إلى مقارنة الفرق في التأثير بين العقارين على ثخن الطبقة المبطنية الداخلية للشرايين العنقية-شملت الدراسة ٦٢ مريضاً من النوع غير المعتمد على الأنسولين في مركز الحكيم للسكري في الفترة بين كانون الثاني ٢٠١١ واذار ٢٠١٢ وكان عمر المصابين بالمتوسط ٥٣,٢ سنة وتوزعوا على ٣٥ من الإناث و ٢٧ من الذكور وبمعدل كتلة الجسم ٢٨,٤ وقد وزع المرضى وبشكل غير محدد على مجموعتين ٣١ استخدموا كليمبريد ٣ ملغم و ٣١ استخدموا ٣ ملغم رابكليدين تم إعادة فحص ثخن الطبقة المبطنية الداخلية للشرايين العنقية بواسطة جهاز الأمواج فوق الصوتية بعد ٦ شهور وبعد ١٢ شهراً مع دراسة مستوى الدهون وحساب معدل السكر التراكمي أثبتت النتائج الإحصائية أن عقار رابكليدين أفضل من عقار كليمبريد في خفض ثخن الطبقة المبطنية الداخلية للشرايين العنقية.

## Introduction

Multiple risk factors interventional trial (MRFIT) suggested that the prevalence of atherosclerosis is two to three times in diabetic patients than in those without diabetes[1]. Atherosclerosis is the cause of morbidity in 70% of patients with type 2 DM [2]. Hyperglycemia induces endothelial dysfunction along with hypercoagulability potential of DM causes acceleration in the process of atherosclerosis complications. DM enhances the plaque vulnerability, increases the inflammation and neovascularization. Post mortem studies provided multiple observational evidences related to the increased abundance of macrophages, neovessels in diabetic atheroma. Increased inflammation induces the increased in heme oxygenase -1( HO-1) in DM. In order to attenuate the oxidative stress HO-1 induction is modulated by the peroxisome proliferation activator receptors (PPAR)[4]. PPAR alpha and PPAR gamma and ligands and advanced glycation end products (AGE) associated with DM (Evans et al, 2004)[3]. DM with increased proinflammation and proatherogenic and additional oxidative stress with AGE proteins facilitates increased need for HO-1 in DM plaques. Studies from Hisayama cohort study clinical trial and autopsy derived plaques from DM associated human atherosclerosis indicates a significant HO-1 proteins expression when compare to non DM (Song et al.2009). This is due to impending need of HO-1 to balance and counter regulate the oxidant stress and the inflammatory process which is apparently mediated by the HO-1 enzymes system against the oxidative and inflammatory activation .The vessel wall responds to antagonize the deleterious effects of heme at three different levels Extracellular, Cellular

membrane and Intracellular level. In ordinary condition endothelium is resistant to the leukocytes adhesion but hypercholesteremia promotes leukocyte adhesion to endothelium. Oxidized LDL reduces intracellular concentration of nitrous oxide (NO) and cause endothelial activation[2]. Angiotensin II has an important role in endothelial dysfunction it opposes NO action and increases production of reactive oxygen species (ROS) which increases expression of proinflammation cytokines like 1LK, monocyte-chemottract protein-1(MCP-1) and also unregulated vascular adhesion molecule-1 (VCAM-1). These endothelial coupled with elevated acute phase protein (CRP) level set the stage of initiating and progression of atherosclerosis promoting inflammation within the vessel wall[2]. There are four theories to explain the association of hyperglycemia with atherosclerosis .First is the increased polyol pathway. Second increased advanced glycation end products (AGE).Third is the activation of protein kinase C (PKC) isoforms and fourth increased hexosamine pathway flux. Measurement of the carotid intima media thickness CIMT is a noninvasive test where the lining of the carotid arteries is measured with the use of B-mode ultrasound. The intima is the innermost layer of the artery, and the media is the middle layer of the artery. CIMT persisted as an independent in the three cohorts after full or partial adjustment for Framingham risk factors[6].The meta analysis demonstrated that studies showing positive association between CIMT and plasma level of C-reactive protein(CRP)or fibrinogen are in majority[13].Lorenz et al 2007 conducted a systematic review of the literatures to provide clinical cardiovascular end points. The review found that CIMT is a strong predictor of future vascular events but it did not

consistently improve the risk classification of individual. American Diabetes Association and American College of cardiology foundation report included the following statement regarding CIMT measurement.(The presence of so called subclinical vascular disease may be determined by measuring calcification, CIMT or the ankle-brachial index. Patients with documented subclinical atherosclerosis are at increased cardiovascular disease risk and may considered candidates for more aggressive therapy)<sup>7</sup> The recommendation of American Society of Echo cardiology according to (Stein, et al,2008) concluded that measuring CIMT and identifying carotid plaque by ultrasound are most useful for refining cardiovascular risk assessment in patients at intermediate cardiovascular risk( Framingham risk) score 6-20% without established coronary heart disease, peripheral arterial disease, cerebral vascular disease, diabetes mellitus or aortic aneurysm[20]. repaglinide is antidiabetic oral agent of the new glidine class with insulin tropic activity [10], Its action on insulin secretion is more rapid and shorter than that of sulphonylurea compounds. Glimepiride is an oral blood glucose lowering drug of the sulphonylurea class. It is classified as third generation, act as secretagogue and it increases activity of intracellular insulin receptors[8].

### **Patients and Methods**

62 patents NIDDM all had their recording files in Al Hakeem diabetic center in Sadar teaching hospital in Najaf enrolled in the study from January 2011 to March 2012 and the patients were randomized either to receive either a fix dose of repaglinide 3mg/day or 3mg/day glimepiride for one year and review was done after 6 months from start of the study ,and then after 12 months. The parameters used in

the study included CIMT of both internal carotid and common carotid ,HbA<sub>1c</sub>, LDL, TG, HDL(high-density lipoprotein), Serum cholesterol, CRP, Blood urea and Serum Creatinine, Blood pressure and protienurea. Inclusion criteria were previously known type 2 diabetic patients treated with oral hypoglycemic agents , age 35-75 years, HbA<sub>1c</sub>>6.6.Exclusion criteria include significant elevation in the hepatic enzyme alanine aminotransferases elevation >2.5 folds in gender specific normal value or renal disease (serum Creatinine >1.2).absence of congestive heart failure (NYHA class2 to 4), cigarette smoking, absence of aortic stenosis or carotid arterial obstruction .CIMT was evaluated with high resolution ultrasonic Doppler type (Toshiba Xavio) (Figure 1).

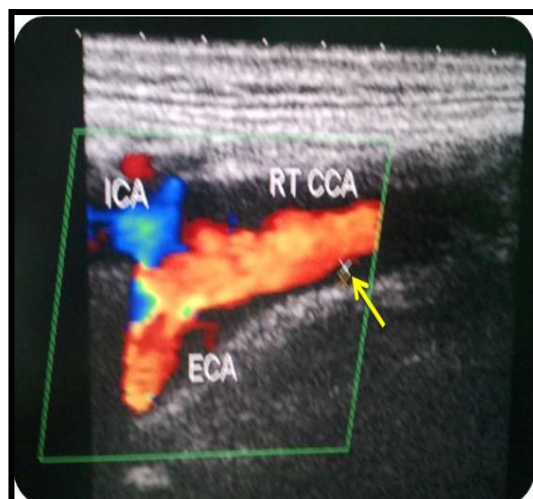


Figure (1) ultrasonic Doppler study of right common Carotid Artery(RTCCA) intima-media thickness.

ICA, Internal Carotid Artery; ECA, External Carotid Artery

Every patient was evaluated 3 times by a single operator at intervals of 6 months and 12 months. On a longitudinal two dimensional ultrasound image of the carotid artery, the anterior (near) and posterior (far) wall of the carotid artery are displaced as two bright white lines separated by hypoechogenic space. The distance between the leading edge of the first

bright line of the far wall (luminal-intimal interface) and the leading edge of the second bright line (media-adventia interface) indicates the intima-media thickness, the procedure was repeated on both sides. The interfaces of the distal common carotid artery were marked across a length of 10 mm. The beginning of dilatation of distal common carotid artery served as reference point for start of the measurement. At least 3 readings were taken and the average of 3 readings of CIMT was taken for evaluation the CIMT of both right and left sides was

calculated and average of 2 values was also taken.

Photometric HbA<sub>1c</sub> assay was done by mixing 100µL whole blood with 500uL glycine for 10 minutes then 20uL from the mixture is taken and added to it 5 mmol water and tested with 410 nanometer photometry.

The lipid profile was studied by ARCHITECT plus Abbott type instrument. All statistical analysis was obtained using statistically package for social sciences (SPSS) version 20 computer software. All data of each set expressed as mean±SD.

### Patient data according to age groups

#### Group 1 the age of patient (35-44) year

| sex | BMI   | HbA <sub>1c</sub> | CRP  | BP     | UREA | CR  | CHOL | TG  | HDL | LDL | PU  | Lt<br>IC<br>MIT | RT<br>IC<br>MIT | M<br>IC<br>MIT | LT<br>CC<br>MIT | RT<br>CC<br>MIT | M<br>CC<br>MIT | D |
|-----|-------|-------------------|------|--------|------|-----|------|-----|-----|-----|-----|-----------------|-----------------|----------------|-----------------|-----------------|----------------|---|
| F   | 28.4  | 8.2               | 4.6  | 130/80 | 32   | 0.8 | 225  | 130 | 40  | 110 | -ve | 0.07            | 0.07            | 0.07           | 0.07            | 0.07            | 0.07           | 2 |
| F   | 31.2  | 8.3               | 8.6  | 130/80 | 34   | 0.8 | 180  | 170 | 45  | 85  | -ve | 0.07            | 0.07            | 0.07           | 0.07            | 0.08            | 0.075          | 1 |
| F   | 23.6  | 6.8               | 3.1  | 130/80 | 29   | 0.9 | 225  | 175 | 47  | 105 | -ve | 0.06            | 0.05            | 0.055          | 0.05            | 0.05            | 0.05           | 1 |
| F   | 31.5  | 9.2               | 4.1  | 120/80 | 32   | 0.8 | 187  | 150 | 44  | 95  | -ve | 0.05            | 0.05            | 0.05           | 0.05            | 0.05            | 0.05           | 2 |
| F   | 26.6  | 8.4               | 5.1  | 130/80 | 34   | 0.7 | 193  | 175 | 47  | 105 | -ve | 0.06            | 0.06            | 0.06           | 0.06            | 0.06            | 0.06           | 1 |
| F   | 26.2  | 7.5               | 2.3  | 120/80 | 31   | 0.8 | 175  | 121 | 34  | 80  | -ve | 0.09            | 0.09            | 0.09           | 0.08            | 0.08            | 0.08           | 1 |
| M   | 27.1  | 9.0               | 5.5  | 120/80 | 36   | 0.8 | 230  | 180 | 36  | 115 | -ve | 0.07            | 0.07            | 0.07           | 0.07            | 0.07            | 0.07           | 2 |
| F   | 25.9  | 7.8               | 3.6  | 140/83 | 30   | 0.8 | 210  | 348 | 38  | 120 | -ve | 0.06            | 0.07            | 0.65           | 0.07            | 0.07            | 0.07           | 1 |
| M   | 34.37 | 8.1               | 4.4  | 120/70 | 28   | 0.6 | 205  | 218 | 30  | 110 | -ve | 0.06            | 0.06            | 0.06           | 0.06            | 0.06            | 0.06           | 2 |
| F   | 30.7  | 19.2              | 3.3  | 120/80 | 35   | 0.8 | 270  | 230 | 35  | 105 | -ve | 0.06            | 0.06            | 0.06           | 0.06            | 0.06            | 0.06           | 1 |
| M   | 24.82 | 10.8              | 4.5  | 120/70 | 28   | 0.8 | 260  | 160 | 42  | 110 | -ve | 0.08            | 0.07            | 0.075          | 0.08            | 0.08            | 0.08           | 2 |
| M   | 42.1  | 8.9               | 402  | 150/90 | 30   | 1   | 240  | 140 | 40  | 95  | -ve | 0.06            | 0.06            | 0.06           | 0.06            | 0.065           | 0.062          | 2 |
| M   | 24.3  | 12.8              | 2.4  | 110/80 | 30   | 6.6 | 210  | 160 | 35  | 95  | -ve | 0.08            | 0.09            | 0.08           | 0.08            | 0.09            | 0.09           | 1 |
| F   | 24.2  | 14                | 4.6  | 120/80 | 26   | 0.5 | 180  | 135 | 42  | 85  | -ve | 0.06            | 0.07            | 0.065          | 0.07            | 0.07            | 0.07           | 1 |
| M   | 23.6  | 9.2               | 3.2  | 110/70 | 28   | 0.6 | 170  | 110 | 35  | 110 | -ve | 0.03            | 0.03            | 0.03           | 0.03            | 0.03            | 0.03           | 1 |
| F   | 24.2  | 8.8               | 4.1  | 110/70 | 26   | 0.7 | 190  | 170 | 45  | 96  | -ve | 0.07            | 0.06            | 0.65           | 0.08            | 0.06            | 0.07           | 2 |
| M   | 26.5  | 12.5              | 12.3 | 140/90 | 28   | 0.8 | 220  | 205 | 32  | 125 | -ve | 0.09            | 0.09            | 0.09           | 0.08            | 0.08            | 0.08           | 1 |
| F   | 25.1  | 10.2              | 4.6  | 120/85 | 26   | 0.4 | 280  | 170 | 38  | 110 | -ve | 0.07            | 0.06            | 0.65           | 0.08            | 0.08            | 0.08           | 2 |
| F   | 21.1  | 8.1               | 4.8  | 110/70 | 28   | 0.6 | 180  | 175 | 35  | 85  | -ve | 0.06            | 0.06            | 0.06           | 0.15            | 0.06            | 0.055          | 1 |
| M   | 29.07 | 13.4              | 17.2 | 130/85 | 28   | 0.9 | 220  | 135 | 35  | 105 | -ve | 0.07            | 0.07            | 0.07           | 0.08            | 0.08            | 0.08           | 2 |
| F   | 23.7  | 8.2               | 2.3  | 110/70 | 28   | 0.6 | 182  | 115 | 40  | 95  | -ve | 0.06            | 0.06            | 0.06           | 0.06            | 0.06            | 0.06           | 2 |
| M   | 26    | 12.8              | 8    | 120/75 | 27   | 0.8 | 235  | 168 | 32  | 112 | -ve | 0.07            | 0.07            | 0.06           | 0.06            | 0.06            | 0.06           | 1 |
| M   | 28.6  | 10.5              | 15.2 | 120/80 | 26   | 0.6 | 265  | 135 | 35  | 115 | -ve | 0.06            | 0.06            | 0.06           | 0.06            | 0.06            | 0.06           | 1 |

### Group 2 the age of patient (45-54) year

| sex | BMI       | HbA <sub>1c</sub> | CRP  | BP      | UREA | CR   | CHOL | TG  | HDL | LDL | PU  | Lt<br>IC<br>MIT | RT<br>IC<br>MIT | M<br>IC<br>MIT | LT<br>CC<br>MIT | RT<br>CC<br>MIT | M<br>CC<br>MIT | D |
|-----|-----------|-------------------|------|---------|------|------|------|-----|-----|-----|-----|-----------------|-----------------|----------------|-----------------|-----------------|----------------|---|
| M   | 25.6      | 8.4               | 6.6  | 120/80  | 30   | 0.6  | 220  | 170 | 35  | 110 | -ve | 0.08            | 0.07            | 0.075          | 0.08            | 0.08            | 0.08           | 1 |
| M   | 30.9      | 7.1               | 2.1  | 120/80  | 35   | 0.9  | 228  | 118 | 35  | 105 | -ve | 0.06            | 0.07            | 0.065          | 0.07            | 0.08            | 0.075          | 1 |
| M   | 26.4      | 8.9               | 4.6  | 130/80  | 32   | 0.8  | 106  | 170 | 34  | 110 | -ve | 0.06            | 0.06            | 0.06           | 0.06            | 0.06            | 0.06           | 2 |
| F   | 31.9<br>6 | 12.1              | 4.3  | 140/80  | 32   | 0.6  | 222  | 164 | 44  | 95  | -ve | 0.09            | 0.09            | 0.09           | 0.08            | 0.08            | 0.08           | 2 |
| F   | 25.7<br>8 | 11.2              | 136  | 130/80  | 18   | 0.83 | 193  | 138 | 40  | 110 | -ve | 0.09            | 0.08            | 0.085          | 0.08            | 0.08            | 0.08           | 2 |
| M   | 2.5       | 8.2               | 3.2  | 120/80  | 32   | 0.8  | 220  | 165 | 40  | 105 | -ve | 0.08            | 0.09            | 0.08           | 0.08            | 0.07            | 0.075          | 1 |
| M   | 27.3      | 10.2              | 4.6  | 120/70  | 26   | 0.8  | 240  | 210 | 34  | 130 | -ve | 0.08            | 0.08            | 0.09           | 0.08            | 0.08            | 0.08           | 1 |
| F   | 26.1      | 8.4               | 6.1  | 120/85  | 28   | 0.8  | 205  | 180 | 43  | 92  | -ve | 0.08            | 0.07            | 0.75           | 0.09            | 0.09            | 0.09           | 1 |
| F   | 28.7      | 9.2               | 4.1  | 110/70  | 32   | 0.7  | 230  | 230 | 34  | 130 | -ve | 0.09            | 0.08            | 0.85           | 0.09            | 0.09            | 0.09           | 2 |
| F   | 27.7      | 10.2              | 5.21 | 130/80  | 28   | 0.8  | 230  | 170 | 35  | 105 | -ve | 0.09            | 0.09            | 0.09           | 0.090           | 0.09            | 0.09           | 2 |
| F   | 26.9      | 12.5              | 16.3 | 160/110 | 32   | 0.8  | 260  | 160 | 42  | 110 | -ve | 0.09            | 0.09            | 0.09           | 0.09            | 0.09            | 0.09           | 2 |
| F   | 24.8      | 9.2               | 2.4  | 120/80  | 36   | 0.7  | 240  | 110 | 42  | 105 | -ve | 0.10            | 0.10            | 0.11           | 0.11            | 0.11            | 0.11           | 1 |
| M   | 25.1      | 11.4              | 4.6  | 130/80  | 34   | 0.8  | 220  | 120 | 42  | 90  | -ve | 0.11            | 0.11            | 0.10           | 0.10            | 0.10            | 0.10           | 2 |
| F   | 27.6      | 10.3              | 5.4  | 120/75  | 28   | 0.8  | 230  | 105 | 34  | 90  | -ve | 0.06            | 0.065           | 0.06           | 0.06            | 0.06            | 0.06           | 1 |
| M   | 28.1      | 9.4               | 4.6  | 105/70  | 26   | 0.7  | 225  | 121 | 32  | 85  | -ve | 0.09            | 0.08            | 0.08           | 0.09            | 0.09            | 0.09           | 2 |
| M   | 27        | 10.3              | 7.4  | 110/70  | 32   | 0.8  | 230  | 120 | 34  | 84  | -ve | 0.07            | 0.07            | 0.07           | 0.07            | 0.07            | 0.07           | 1 |
| M   | 26.2      | 10.6              | 5.3  | 120/70  | 38   | 1.2  | 210  | 110 | 38  | 80  | -ve | 0.09            | 0.09            | 0.09           | 0.09            | 0.09            | 0.09           | 2 |

### Group 3 the age of patient (55-64)year

| sex | BMI   | HbA <sub>1c</sub> | CRP  | BP     | UREA | CR  | CHOL | TG  | HDL | LDL | PU  | Lt<br>IC<br>MIT | RT<br>IC<br>MIT | M<br>IC<br>MIT | LT<br>CC<br>MIT | RT<br>CC<br>MIT | M<br>CC<br>MIT | D |
|-----|-------|-------------------|------|--------|------|-----|------|-----|-----|-----|-----|-----------------|-----------------|----------------|-----------------|-----------------|----------------|---|
| M   | 26.7  | 10.3              | 4.8  | 130/90 | 32   | 0.9 | 210  | 180 | 42  | 110 | -ve | 0.11            | 0.11            | 0.11           | 0.10            | 0.10            | 0.10           | 1 |
| M   | 26.5  | 13.4              | 8.3  | 110/70 | 28   | 0.8 | 220  | 220 | 32  | 120 | -ve | 0.09            | 0.09            | 0.09           | 0.09            | 0.09            | 0.09           | 2 |
| M   | 33.6  | 7.6               | 3.3  | 130/80 | 24   | 0.6 | 190  | 130 | 45  | 80  | -ve | 0.09            | 0.09            | 0.09           | 0.09            | 0.09            | 0.09           | 1 |
| M   | 28.06 | 7.5               | 7.6  | 120/80 | 32   | 0.8 | 240  | 145 | 40  | 110 | -ve | 0.06            | 0.06            | 0.06           | 0.07            | 0.07            | 0.07           | 1 |
| F   | 26.2  | 10.2              | 15.2 | 120/80 | 32   | 0.8 | 263  | 217 | 42  | 115 | -ve | 0.10            | 0.11            | 0.105          | 0.11            | 0.11            | 0.11           | 2 |
| F   | 24.3  | 8.5               | 6.2  | 120/80 | 28   | 0.6 | 220  | 170 | 40  | 120 | -ve | 0.06            | 0.07            | 0.065          | 0.07            | 0.07            | 0.07           | 2 |
| F   | 27.3  | 8.5               | 9.1  | 130/70 | 35   | 0.9 | 265  | 406 | 30  | 120 | -ve | 0.11            | 0.11            | 0.11           | 0.12            | 0.12            | 0.12           | 1 |
| F   | 30.6  | 14.1              | 12   | 140/80 | 35   | 0.9 | 314  | 210 | 33  | 220 | -ve | 0.08            | 0.08            | 0.08           | 0.09            | 0.09            | 0.09           | 2 |
| M   | 31.8  | 10.5              | 3.2  | 130/90 | 32   | 0.8 | 269  | 210 | 40  | 140 | -ve | 0.10            | 0.10            | 0.10           | 0.10            | 0.11            | 0.105          | 2 |
| M   | 25.9  | 11.2              | 6    | 130/80 | 32   | 0.9 | 224  | 152 | 34  | 110 | -ve | 0.08            | 0.08            | 0.09           | 0.09            | 0.09            | 0.09           | 2 |
| F   | 25.7  | 10.7              | 2    | 120/80 | 28   | 0.8 | 210  | 110 | 36  | 90  | -ve | 0.07            | 0.07            | 0.07           | 0.07            | 0.07            | 0.07           | 2 |
| F   | 27.6  | 12.2              | 6.6  | 110/70 | 34   | 0.9 | 220  | 105 | 35  | 95  | -ve | 0.09            | 0.09            | 0.09           | 0.09            | 0.09            | 0.09           | 1 |
| F   | 27.1  | 12.6              | 6.6  | 110/60 | 37   | 0.8 | 270  | 130 | 36  | 85  | -ve | 0.11            | 0.11            | 0.10           | 0.10            | 0.10            | 0.10           | 1 |
| M   | 23.9  | 10.9              | 2.2  | 130/70 | 30   | 0.9 | 190  | 110 | 34  | 75  | -ve | 0.10            | 0.10            | 0.09           | 0.09            | 0.09            | 0.09           | 1 |
| F   | 26.78 | 7.5               | 2.5  | 100/60 | 32   | 0.8 | 210  | 160 | 35  | 110 | -ve | 0.09            | 0.09            | 0.09           | 0.89            | 0.80            | 0.095          | 1 |
| M   | 28.7  | 10.2              | 4.1  | 140/80 | 30.2 | 0.8 | 102  | 110 | 32  | 95  | -ve | 0.08            | 0.08            | 0.08           | 0.09            | 0.09            | 0.09           | 2 |
| M   | 24.6  | 10.8              | 3.2  | 110/60 | 32   | 0.7 | 240  | 105 | 38  | 85  | -ve | 0.09            | 0.09            | 0.09           | 0.09            | 0.09            | 0.09           | 2 |
| F   | 26.5  | 12.1              | 7.6  | 130/80 | 36   | 0.9 | 220  | 110 | 32  | 80  | -ve | 0.08            | 0.08            | 0.07           | 0.07            | 0.07            | 0.07           | 2 |

### Group 4 the age of patient (65-75)year

| sex | BMI  | HbA <sub>1c</sub> | CRP  | BP     | UREA | CR  | CHOL | TG  | HDL | LDL | PU  | Lt<br>IC<br>MIT | RT<br>IC<br>MIT | M<br>IC<br>MIT | LT<br>CC<br>MIT | RT<br>CC<br>MIT | M<br>CC<br>MIT | D |
|-----|------|-------------------|------|--------|------|-----|------|-----|-----|-----|-----|-----------------|-----------------|----------------|-----------------|-----------------|----------------|---|
| M   | 23.8 | 8.3               | 12.5 | 160/80 | 26   | 0.8 | 220  | 160 | 35  | 90  | -ve | 0.12            | 0.1             | 0.11           | 0.10            | 0.12            | 0.11           | 2 |
| M   | 25.4 | 9.4               | 8.2  | 120/70 | 29   | 0.8 | 230  | 180 | 35  | 115 | -ve | 0.07            | 0.07            | 0.07           | 0.08            | 0.08            | 0.08           | 1 |
| F   | 20.5 | 8.6               | 4.3  | 120/80 | 26   | 0.8 | 205  | 140 | 30  | 110 | -ve | 0.06            | 0.08            | 0.07           | 0.06            | 0.07            | 0.065          | 1 |
| F   | 27.7 | 12.5              | 15.3 | 140/80 | 41   | 0.5 | 167  | 138 | 32  | 90  | -ve | 0.06            | 0.07            | 0.065          | 0.06            | 0.06            | 0.06           | 2 |

**BMI**, body mass index ;**HbA<sub>1c</sub>**, hemoglobin A1c ;**CRP**, C-reactive protein ;**BP**, Blood pressure ;**CR**, Serum Creatinine ;**CHOL**, cholesterol ; **TG**, Triglyceride ;**HDL**, High-density lipoprotein ;**LDL**, Low-density lipoprotein ;**PU**, protienurea ;**Lf**, left ;**RT**, right ;**IC**, internal carotid ; **CC**, common carotid ;**MIT**, intima-media thickness ;**M**, mean ;**D<sub>1</sub>**, repaglinide ;**D<sub>2</sub>**, glimepiride .

### Result

In comparing different pairs of patients and as shown in the tables and in between drug 1(repaglinide) and drug 2 (glimepiride) and after 12 months of treatment and in different parameters. the reduction in the CIMT of left internal carotid with p value

<0.0001 and it is a significant one ,the reduction in the CIMT of the right common carotid artery is more with the repaglinide with p value <0.0019 and it is a significant . the reduction in the level of HbA<sub>1c</sub> more with rapiglinide still not a significant with p value 0.127 , the same for CPR with p

value 0.137 and LDL with p value 0.317 ,for TG p value 0.939 and for s. cholesterol p 0.445 all not a significant.

**Table 1** Paired T test Drug 1(repaglinide) baseline and after 6 months

**Paired Samples Test**

|         |                                         | Paired Differences |                |                    |                            |           | t       | df | Sig. (2-tailed) |
|---------|-----------------------------------------|--------------------|----------------|--------------------|----------------------------|-----------|---------|----|-----------------|
|         |                                         | Mean               | Std. Deviation | Std. Error<br>Mean | 95% Confidence Interval of |           |         |    |                 |
|         |                                         |                    |                |                    | the Difference             |           |         |    |                 |
|         |                                         |                    |                |                    | Lower                      | Upper     |         |    |                 |
| Pair 1  | HbA <sub>1c</sub> - HbA <sub>1c</sub> 6 | 2.52258            | 2.05341        | .36880             | 1.76939                    | 3.27578   | 6.840   | 30 | .000            |
| Pair 2  | CRP - CRP6                              | 1.91613            | 3.26058        | .58562             | .72014                     | 3.11212   | 3.272   | 30 | .003            |
| Pair 3  | Urea - Urea6                            | 1.09677            | 3.96951        | .71294             | -.35925-                   | 2.55280   | 1.538   | 30 | .134            |
| Pair 4  | CR - CR6                                | .18710             | 1.08436        | .19476             | -.21065-                   | .58484    | .961    | 30 | .344            |
| Pair 5  | Choll - Choll6                          | 26.70968           | 39.02580       | 7.00924            | 12.39490                   | 41.02446  | 3.811   | 30 | .001            |
| Pair 6  | Trig - Trig6                            | -6.41935-          | 79.44129       | 14.26808           | -35.55865-                 | 22.71994  | -.450-  | 30 | .656            |
| Pair 7  | HDL - HDL6                              | 16.58065           | 37.34950       | 6.70817            | 2.88074                    | 30.28055  | 2.472   | 30 | .019            |
| Pair 8  | LDL - LDL6                              | -17.70968-         | 43.51796       | 7.81606            | -33.67219-                 | -1.74716- | -2.266- | 30 | .031            |
| Pair 9  | LtICMIT - LtICMIT6                      | .00452             | .00961         | .00173             | .00099                     | .00804    | 2.618   | 30 | .014            |
| Pair 10 | RtICMIT - RtICMIT6                      | .00242             | .01802         | .00324             | -.00419-                   | .00903    | .747    | 30 | .461            |
| Pair 11 | MICMIT - MICMIT6                        | .04468             | .15708         | .02821             | -.01294-                   | .10230    | 1.584   | 30 | .124            |
| Pair 12 | LtCCMIT - LtCCMIT6                      | .00748             | .02344         | .00421             | -.00112-                   | .01608    | 1.777   | 30 | .086            |
| Pair 13 | RtCCMIT -<br>RtCCMIT6                   | .02613             | .12917         | .02320             | -.02125-                   | .07351    | 1.126   | 30 | .269            |
| Pair 14 | MCCMIT - MCCMIT6                        | -.02032-           | .12747         | .02289             | -.06708-                   | .02643    | -.888-  | 30 | .382            |

**Table 2** Paired T test Drug 1(repaglinide) between after 6 months and after 12 months  
**Pired Samples Test**

|         |                                            | Paired Differences |                   |                    |                         |          | t      | df | Sig. (2-tailed) |
|---------|--------------------------------------------|--------------------|-------------------|--------------------|-------------------------|----------|--------|----|-----------------|
|         |                                            | Mean               | Std.<br>Deviation | Std. Error<br>Mean | 95% Confidence Interval |          |        |    |                 |
|         |                                            |                    |                   |                    | of the Difference       |          |        |    |                 |
|         |                                            |                    |                   |                    | Lower                   | Upper    |        |    |                 |
| Pair 1  | HbA <sub>1c</sub> 6 - HbA <sub>1c</sub> 12 | .47419             | 1.10694           | .19881             | .06817                  | .88022   | 2.385  | 30 | .024            |
| Pair 2  | CRP6 - CRP12                               | .56452             | 1.82475           | .32773             | -.10481-                | 1.23384  | 1.722  | 30 | .095            |
| Pair 3  | Urea6 - Urea12                             | -.06452-           | 2.59404           | .46590             | -1.01602-               | .88698   | -.138- | 30 | .891            |
| Pair 4  | CR6 - CR12                                 | -6.08968-          | 33.96563          | 6.10041            | -18.54837-              | 6.36901  | -.998- | 30 | .326            |
| Pair 5  | Choll6 - Choll12                           | -2.32258-          | 21.30162          | 3.82588            | -10.13608-              | 5.49092  | -.607- | 30 | .548            |
| Pair 6  | Trig6 - Trig12                             | 2.80000            | 24.89343          | 4.54490            | -6.49536-               | 12.09536 | .616   | 29 | .543            |
| Pair 7  | HDL6 - HDL12                               | .51613             | 5.47644           | .98360             | -1.49265-               | 2.52490  | .525   | 30 | .604            |
| Pair 8  | LDL6 - LDL12                               | -22.74194-         | 139.92450         | 25.13118           | -74.06665-              | 28.58278 | -.905- | 30 | .373            |
| Pair 9  | LtICMIT6 -<br>LtICMIC12                    | .00323             | .01045            | .00188             | -.00061-                | .00706   | 1.718  | 30 | .096            |
| Pair 10 | RtICMIT6 -<br>RtICMIC12                    | .00387             | .01116            | .00200             | -.00022-                | .00796   | 1.931  | 30 | .063            |
| Pair 11 | MICMIT6 -<br>MICMIT12                      | -.02113-           | .14123            | .02537             | -.07293-                | .03067   | -.833- | 30 | .411            |
| Pair 12 | LtCCMIT6 -<br>LtCCMIT12                    | .02348             | .14741            | .02647             | -.03058-                | .07755   | .887   | 30 | .382            |
| Pair 13 | RtCCMIT6 -<br>RtCCMIT12                    | -.01484-           | .10188            | .01830             | -.05221-                | .02253   | -.811- | 30 | .424            |
| Pair 14 | MCCMIT6 -<br>MCCMIT12                      | .01129             | .15962            | .02867             | -.04726-                | .06984   | .394   | 30 | .696            |

**Table 3** Paired T test Drug 1(repaglinide) between baseline and after 12 months

**Paired Samples Test**

|         |                                          | Paired Differences |                   |                    |                         |          | t      | df | Sig. (2-tailed) |
|---------|------------------------------------------|--------------------|-------------------|--------------------|-------------------------|----------|--------|----|-----------------|
|         |                                          | Mean               | Std.<br>Deviation | Std. Error<br>Mean | 95% Confidence Interval |          |        |    |                 |
|         |                                          |                    |                   |                    | of the Difference       |          |        |    |                 |
|         |                                          |                    |                   |                    | Lower                   | Upper    |        |    |                 |
| Pair 1  | HbA <sub>1c</sub> - HbA <sub>1c</sub> 12 | 2.99677            | 2.42274           | .43514             | 2.10811                 | 3.88544  | 6.887  | 30 | .000            |
| Pair 2  | CRP - CRP12                              | 2.48065            | 3.14212           | .56434             | 1.32810                 | 3.63319  | 4.396  | 30 | .000            |
| Pair 3  | Urea - Urea12                            | 1.03226            | 3.75485           | .67439             | -.34503                 | 2.40955  | 1.531  | 30 | .136            |
| Pair 4  | CR - CR12                                | -5.90258           | 34.03895          | 6.11358            | -18.38817               | 6.58301  | -.965  | 30 | .342            |
| Pair 5  | Choll - Choll12                          | 24.38710           | 50.51777          | 9.07326            | 5.85703                 | 42.91716 | 2.688  | 30 | .012            |
| Pair 6  | Trig - Trig12                            | -8.10000           | 91.24516          | 16.65901           | -42.17150               | 25.97150 | -.486  | 29 | .630            |
| Pair 7  | HDL - HDL12                              | 17.09677           | 39.28389          | 7.05559            | 2.68733                 | 31.50622 | 2.423  | 30 | .022            |
| Pair 8  | LDL - LDL12                              | -40.45161          | 146.75168         | 26.35738           | -94.28056               | 13.37734 | -1.535 | 30 | .135            |
| Pair 9  | LtICMIT -                                | .00774             | .01087            | .00195             | .00376                  | .01173   | 3.967  | 30 | .000            |
|         | LtICMIC12                                |                    |                   |                    |                         |          |        |    |                 |
| Pair 10 | RtICMIT -                                | .00629             | .02074            | .00372             | -.00132                 | .01390   | 1.689  | 30 | .102            |
|         | RtICMIC12                                |                    |                   |                    |                         |          |        |    |                 |
| Pair 11 | MICMIT -                                 | .02355             | .12801            | .02299             | -.02341                 | .07050   | 1.024  | 30 | .314            |
|         | MICMIT12                                 |                    |                   |                    |                         |          |        |    |                 |
| Pair 12 | LtCCMIT -                                | .03097             | .14871            | .02671             | -.02358                 | .08552   | 1.159  | 30 | .255            |
|         | LtCCMIT12                                |                    |                   |                    |                         |          |        |    |                 |
| Pair 13 | RtCCMIT -                                | .01129             | .16939            | .03042             | -.05084                 | .07342   | .371   | 30 | .713            |
|         | RtCCMIT12                                |                    |                   |                    |                         |          |        |    |                 |
| Pair 14 | MCCMIT -                                 | -.00903            | .08758            | .01573             | -.04116                 | .02309   | -.574  | 30 | .570            |
|         | MCCMIT12                                 |                    |                   |                    |                         |          |        |    |                 |

**Table 4** Paired T test Drug 2 (glimepiride) baseline and after 6 months  
**Paired Samples Test**

|         |                                         | Paired Differences |                   |                    |                         |          | t      | df | Sig. (2-tailed) |
|---------|-----------------------------------------|--------------------|-------------------|--------------------|-------------------------|----------|--------|----|-----------------|
|         |                                         | Mean               | Std.<br>Deviation | Std. Error<br>Mean | 95% Confidence Interval |          |        |    |                 |
|         |                                         |                    |                   |                    | of the Difference       |          |        |    |                 |
|         |                                         |                    |                   |                    | Lower                   | Upper    |        |    |                 |
| Pair 1  | HbA <sub>1c</sub> - HbA <sub>1c</sub> 6 | 3.22581            | 1.56076           | .28032             | 2.65331                 | 3.79830  | 11.508 | 30 | .000            |
| Pair 2  | CRP - CRP6                              | 2.66333            | 6.41751           | 1.17167            | .26699                  | 5.05967  | 2.273  | 29 | .031            |
| Pair 3  | Urea - Urea6                            | -.05806            | 4.48678           | .80585             | -1.70383                | 1.58770  | -.072  | 30 | .943            |
| Pair 4  | CR - CR6                                | -.07000            | .18520            | .03326             | -.13793                 | -.00207  | -2.104 | 30 | .044            |
| Pair 5  | Choll - Choll6                          | 27.22581           | 39.97642          | 7.17998            | 12.56234                | 41.88927 | 3.792  | 30 | .001            |
| Pair 6  | Trig - Trig6                            | -17.19355          | 65.06787          | 11.68653           | -41.06064               | 6.67354  | -1.471 | 30 | .152            |
| Pair 7  | HDL - HDL6                              | 16.09677           | 35.56436          | 6.38755            | 3.05166                 | 29.14189 | 2.520  | 30 | .017            |
| Pair 8  | LDL - LDL6                              | -15.93548          | 47.81418          | 8.58768            | -33.47387               | 1.60290  | -1.856 | 30 | .073            |
| Pair 9  | LtICMIT -                               | .01323             | .02468            | .00443             | .00417                  | .02228   | 2.983  | 30 | .006            |
|         | LtICMIT6                                |                    |                   |                    |                         |          |        |    |                 |
| Pair 10 | RtICMIT -                               | .00581             | .00992            | .00178             | .00217                  | .00945   | 3.258  | 30 | .003            |
|         | RtICMIT6                                |                    |                   |                    |                         |          |        |    |                 |
| Pair 11 | MICMIT - MICMIT6                        | .06871             | .19318            | .03470             | -.00215                 | .13957   | 1.980  | 30 | .057            |
| Pair 12 | LtCCMIT -                               | .00419             | .01858            | .00334             | -.00262                 | .01101   | 1.257  | 30 | .219            |
|         | LtCCMIT6                                |                    |                   |                    |                         |          |        |    |                 |
| Pair 13 | RtCCMIT -                               | .00850             | .00975            | .00178             | .00486                  | .01214   | 4.774  | 29 | .000            |
|         | RtCCMIT6                                |                    |                   |                    |                         |          |        |    |                 |
| Pair 14 | MCCMIT -                                | .00790             | .00920            | .00168             | .00446                  | .01134   | 4.701  | 29 | .000            |
|         | MCCMIT6                                 |                    |                   |                    |                         |          |        |    |                 |

**Table 5** Paired t test drug 2 (glimepiride) between after 6 months and after 12 months

**Paired Samples Test**

|         |                                            | Paired Differences |                   |                    |                            |            | t       | df | Sig. (2-tailed) |
|---------|--------------------------------------------|--------------------|-------------------|--------------------|----------------------------|------------|---------|----|-----------------|
|         |                                            | Mean               | Std.<br>Deviation | Std. Error<br>Mean | 95% Confidence Interval of |            |         |    |                 |
|         |                                            |                    |                   |                    | the Difference             |            |         |    |                 |
|         |                                            |                    |                   |                    | Lower                      | Upper      |         |    |                 |
| Pair 1  | HbA <sub>1c</sub> 6 - HbA <sub>1c</sub> 12 | .34194             | .97015            | .17424             | -.01392-                   | .69779     | 1.962   | 30 | .059            |
| Pair 2  | CRP6 - CRP12                               | 1.40000            | 5.52930           | 1.00951            | -.66467-                   | 3.46467    | 1.387   | 29 | .176            |
| Pair 3  | Urea6 - Urea12                             | .48387             | 3.43386           | .61674             | -.77568-                   | 1.74342    | .785    | 30 | .439            |
| Pair 4  | CR6 - CR12                                 | .01290             | .13599            | .02443             | -.03698-                   | .06279     | .528    | 30 | .601            |
| Pair 5  | Choll6 - Choll12                           | 6.29032            | 23.90843          | 4.29408            | -2.47936-                  | 15.06000   | 1.465   | 30 | .153            |
| Pair 6  | Trig6 - Trig12                             | -3998.50000-       | 21907.31141       | 3999.70955         | -12178.82452-              | 4181.82452 | -1.000- | 29 | .326            |
| Pair 7  | HDL6 - HDL12                               | .41935             | 4.33416           | .77844             | -1.17043-                  | 2.00914    | .539    | 30 | .594            |
| Pair 8  | LDL6 - LDL12                               | 3.87097            | 28.00088          | 5.02911            | -6.39984-                  | 14.14177   | .770    | 30 | .447            |
| Pair 9  | LtICMIT6 -<br>LtICMIC12                    | -.00194-           | .02372            | .00426             | -.01064-                   | .00677     | -.454-  | 30 | .653            |
| Pair 10 | RtICMIT6 -<br>RtICMIC12                    | .00387             | .01116            | .00200             | -.00022-                   | .00796     | 1.931   | 30 | .063            |
| Pair 11 | MICMIT6 -<br>MICMIT12                      | .00435             | .01250            | .00224             | -.00023-                   | .00894     | 1.940   | 30 | .062            |
| Pair 12 | LtCCMIT6 -<br>LtCCMIT12                    | .00419             | .01089            | .00196             | .00020                     | .00819     | 2.145   | 30 | .040            |
| Pair 13 | RtCCMIT6 -<br>RtCCMIT12                    | .00300             | .01119            | .00204             | -.00118-                   | .00718     | 1.469   | 29 | .153            |
| Pair 14 | MCCMIT6 -<br>MCCMIT12                      | -.01267-           | .09082            | .01658             | -.04658-                   | .02125     | -.764-  | 29 | .451            |

**Table 6** Paired t test Drug 2 (glimepiride) between baseline and after 12 months

**Paired Samples Test**

|         |                                          | Paired Differences |                   |                    |                         |          | t       | df | Sig. (2-tailed) |
|---------|------------------------------------------|--------------------|-------------------|--------------------|-------------------------|----------|---------|----|-----------------|
|         |                                          | Mean               | Std.<br>Deviation | Std. Error<br>Mean | 95% Confidence Interval |          |         |    |                 |
|         |                                          |                    |                   |                    | of the Difference       |          |         |    |                 |
|         |                                          |                    |                   |                    | Lower                   | Upper    |         |    |                 |
| Pair 1  | HbA <sub>1c</sub> - HbA <sub>1c</sub> 12 | 3.56774            | 1.82782           | .32829             | 2.89729                 | 4.23819  | 10.868  | 30 | .000            |
| Pair 2  | CRP - CRP12                              | 4.03871            | 4.83843           | .86901             | 2.26396                 | 5.81346  | 4.647   | 30 | .000            |
| Pair 3  | Urea - Urea12                            | .42581             | 4.35362           | .78193             | -1.17111-               | 2.02273  | .545    | 30 | .590            |
| Pair 4  | CR - CR12                                | -.05710-           | .19372            | .03479             | -.12815-                | .01396   | -1.641- | 30 | .111            |
| Pair 5  | Choll - Choll12                          | 33.51613           | 42.63166          | 7.65687            | 17.87871                | 49.15355 | 4.377   | 30 | .000            |
| Pair 6  | Trig - Trig12                            | 17.517-            | 81.983            | 15.223             | 48.702                  | 13.667   | 1.151   | 28 | 0.260           |
| Pair 7  | HDL - HDL12                              | 16.51613           | 36.51746          | 6.55873            | 3.12142                 | 29.91084 | 2.518   | 30 | .017            |
| Pair 8  | LDL - LDL12                              | -12.06452-         | 54.99572          | 9.87752            | -32.23711-              | 8.10808  | -1.221- | 30 | .231            |
| Pair 9  | LtICMIT -                                | .01129             | .01118            | .00201             | .00719                  | .01539   | 5.624   | 30 | .000            |
|         | LtICMIC12                                |                    |                   |                    |                         |          |         |    |                 |
| Pair 10 | RtICMIT -                                | .00968             | .01140            | .00205             | .00550                  | .01386   | 4.728   | 30 | .000            |
|         | RtICMIC12                                |                    |                   |                    |                         |          |         |    |                 |
| Pair 11 | MICMIT -                                 | .07306             | .19509            | .03504             | .00151                  | .14462   | 2.085   | 30 | .046            |
|         | MICMIT12                                 |                    |                   |                    |                         |          |         |    |                 |
| Pair 12 | LtCCMIT -                                | .00839             | .02035            | .00365             | .00092                  | .01585   | 2.295   | 30 | .029            |
|         | LtCCMIT12                                |                    |                   |                    |                         |          |         |    |                 |
| Pair 13 | RtCCMIT -                                | .01306             | .01716            | .00308             | .00677                  | .01936   | 4.239   | 30 | .000            |
|         | RtCCMIT12                                |                    |                   |                    |                         |          |         |    |                 |
| Pair 14 | MCCMIT -                                 | -.00461-           | .08913            | .01601             | -.03730-                | .02808   | -.288-  | 30 | .775            |
|         | MCCMIT12                                 |                    |                   |                    |                         |          |         |    |                 |

**Table 7** Differences between Drug 1(repaglinide) and Drug 2(glimepiride) groups regarding Age, Wt, Ht and BMI

**dependent Samples Test**

|     |                             | Levene's Test for Equality of Variances |      | t-test for Equality of Means |        |                 |                 |                       |                                           |         |
|-----|-----------------------------|-----------------------------------------|------|------------------------------|--------|-----------------|-----------------|-----------------------|-------------------------------------------|---------|
|     |                             | F                                       | Sig. | t                            | df     | Sig. (2-tailed) | Mean Difference | Std. Error Difference | 95% Confidence Interval of the Difference |         |
|     |                             |                                         |      |                              |        |                 |                 |                       | Lower                                     | upper   |
| Age | Equal variances assumed     | .900                                    | .346 | -.812-                       | 60     | .420            | -2.12903-       | 2.62313               | -7.37608-                                 | 3.11801 |
|     | Equal variances not assumed |                                         |      | -.812-                       | 58.158 | .420            | -2.12903-       | 2.62313               | -7.37950-                                 | 3.12143 |
| Wt  | Equal variances assumed     | 1.722                                   | .194 | -1.149-                      | 60     | .255            | -3.45161-       | 3.00505               | -9.46260-                                 | 2.55938 |
|     | Equal variances not assumed |                                         |      | -1.149-                      | 49.860 | .256            | -3.45161-       | 3.00505               | -9.48785-                                 | 2.58463 |
| Ht  | Equal variances assumed     | .297                                    | .588 | .823                         | 60     | .414            | 1.41935         | 1.72509               | -2.03133-                                 | 4.87004 |
|     | Equal variances not assumed |                                         |      | .823                         | 55.417 | .414            | 1.41935         | 1.72509               | -2.03721-                                 | 4.87592 |
| BMI | Equal variances assumed     | .049                                    | .826 | -1.765-                      | 60     | .083            | -2.00839-       | 1.13783               | -4.28439-                                 | .26762  |
|     | Equal variances not assumed |                                         |      | -1.765-                      | 55.055 | .083            | -2.00839-       | 1.13783               | -4.28861-                                 | .27183  |

**Table 8** Independent T test differences between means of variables in Drug 1 and drug 2

| Variables         | Drug 1 |         | Drug 2 |        | P Value  |
|-------------------|--------|---------|--------|--------|----------|
|                   | Mean   | SD      | Mean   | SD     |          |
| HbA <sub>1c</sub> | 2.996  | 2.423   | 3.567  | 1.827  | 0.127    |
| CRP               | 2.480  | 3.142   | 4.038  | 4.838  | 0.137    |
| Urea              | 1.032  | 3.754   | 0.425  | 4.353  | 0.558    |
| CR                | 5.902  | 34.038  | 0.057  | 0.193  | 0.343    |
| Cho.              | 24.387 | 50.517  | 33.516 | 42.631 | 0.445    |
| Trig.             | 8.100  | 91.245  | 17.517 | 81.983 | 0.939    |
| HDL               | 17.096 | 39.283  | 16.516 | 36.517 | 0.952    |
| LDL               | 40.451 | 146.751 | 12.064 | 54.995 | 0.317    |
| Lt ICMIT          | 0.07   | 0.01    | 0.011  | 0.011  | < 0.0001 |
| RICMIT            | 0.006  | 0.020   | 0.0096 | 0.011  | 0.467    |
| MICMIT            | 0.0235 | 0.128   | 0.073  | 0.195  | 0.237    |
| LCCMIT            | 0.030  | 0.148   | 0.008  | 0.020  | 0.415    |
| RCCMIT            | 0.011  | 0.169   | 0.013  | 0.017  | 0.0019   |
| MCCMIT            | 0.009  | 0.087   | 0.004  | 0.089  | 0.823    |

### Discussion

In our study compared repaglinide with glimepiride effect on atherosclerosis in patients presenting with NIDDM, we found that the use of repaglinide as compared with glimepiride is better in reduction the CIMT and the reduction was both with left internal carotid and the right common carotid with p value < 0.005 than glimepiride and the difference in benefit is a significant one. Although this reduction is associated with reduction in LDL level, TG and the

HbA<sub>1c</sub> they were not a significant one so the changes in CIMT were independent to the changes in lipid profile in this study. The duration of the study was one year and was of limited duration because of difficulty in our patients to stick to an appropriate time of test so we lost 8 patients during our study.

Repaglinide affect atherosclerosis in many ways, It affects the postprandial glucose level, Repaglinide interacts with the ATP-sensitive potassium channel so that causing

rapid postprandial hypoglycemia ,so the drug is given with each meal or immediately before to reduce meal-related glucose excursions.[23] in our study the reduction of HbA1C was more with Repaglinide but not significant( The aim in our study was not to reach glycemic control to level HbA1c less 6 to avoid hypoglycemic events) . Repaglinide also reduces endothelial dysfunction in glucose manner.[24] Repaglinide modified liposomes targeted to activated platelet as potential vascular drug delivery system.[15] In a study designed on hypercholesteremic rabbits ,it was found that both glimepiride and repaglinide reduced the atherosclerosis progression by interfering both with inflammatory and oxidative pathways as treatment with both did show significant effect on lipid parameters compare with induced treated rabbits. (this also seen in our study) also it showed significantly reduced elevation in CRP, IL-6,TNF-alpha[15]. In another study it was found that glimepiride prevent development of aortic atherosclerosis in fat fed rabbits, underlining mechanism was explained by inhibition of endothelial cell-mediated LDL oxidation [14]. It was also shown that glimepiride treatment enhances the biosynthesis of nitric mono oxide antioxidant[14]. Both repaglinide and glimepiride induced atherosclerosis protection actions by suppression of inflammation and oxidative stress.[26] The major advantage of repaglinide over glimepiride is their rapid and relatively short duration of action, which may attenuate postprandial glucose excursions and reduce the risk of fasting hypoglycemia.[25]

In our opinion we may get more benefit with extension the duration of the study and to see the effect on cardiovascular risk . We used both drugs and tried not to produce the hypoglycemic events. The age of the

patients was 35-75 years(mean 53years) and we tried to avoid the older age patients so decreased the complication .The aim was not to reach glycemic control to level HbA1c less 6 to avoid hypoglycemic events. One interesting action of repaglinide is by shutting down the ATP-dependent potassium channels in the membrane of beta cell of islet of the pancreas stimulating Calcium influx and induces secretion of insulin and this may explain its better CIMT reduction.[26] It was found that intensive therapy for DM for 6 years decreased the progression of CIMT . Offer best control of blood sugar after pancreatic islet transplantation showed significant reduction in CIMT[19]. The median duration of diabetes in the study was 10 years approximately 35% of them had previous CVD ,the trial concluded that intensive glucose lowering produces no benefit in term of CVD risk reduction and even produces harm in high risk patients with type 2[22]. This was explained by more hypoglycemic events and in special old age patients included in the study. It seems that this is related to changes in lipid profile of the patients .The action to control cardiovascular risk (ACCORD) was designed to assess the impact of tight blood sugar control on CVD events in subjects with type 2DM. There was suggestion that patients who did not have a cardiovascular events before randomized and who had a base line of HbA1c of 8% or less had fewer fatal or nonfatal cardiovascular events with intensive control than with standard control. It was shown that reduction in the postprandial hyperglycemia In type 2 DM diabetic patients is associated with much reduction In atherosclerosis and in CIMT reduction[18]. This last explanation in (ACCORD) study put the Repaglinide better than glimepiride in CIMT reduction as it causes more

postprandial decrease in glucose level.[26]

### **Conclusions and Recommendations**

Repaglinide is better than glimepiride in reduction the CIMT and we need to know the best dose of the drug needed to achieve the best respond and that is by use different dose study program and to for longer duration.

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