Repaglinide versus Metformin in controlling post-prandial hyperglycemia in type II diabetics.

Background:
Metformin is a well known anti-diabetic agent, Repaglinide is a new insulin secretagogues.

Objective:
Is to compare between Repaglinide and Metformin in controlling post-prandial hyperglycemia in type II diabetics.

Design:
cross-sectional randomized clinical study.

Patients and Methods:
patients with type II diabetes are randomly divided into 2 groups [ each group contain 25 patients], 1st group patients were already on 1 mg Repaglinide twice daily 10 minutes before meal , 2nd group patients were already on 500 mg Metformin twice daily immediately after meal, for each patient ,2hrs post –prandial blood sugar was done.

Results:
The average post-prandial blood sugar in patients taking Repaglinide was [172.22 mg/dl] ± SEM[1.22] [ range of blood sugar was 127 mg/dl – 170 mg/dl ] , while the
average post-prandial blood sugar in patients taking Metformin was [169.28 mg/dl] with SEM [1.63] [range of blood sugar was 153 mg/dl-186 mg/dl], independent T-test was done which revealed no significant difference between Repaglinide and Metformin in controlling post-prandial hyperglycemia[p>0.05].

**Conclusion and Recommendation:**
there is no significant difference between Repaglinide and Metformin in controlling post-prandial hyperglycemia in type II diabetics and further studies to evaluate cost-effectiveness and cardio-vascular risk reduction of both drugs are needed.

**Introduction:**
Several longitudinal studies have shown a relationship between meal-time glycemic excursion and development of cardio-vascular disease[1,2]. In light of such evidence a strong reduction in post-prandial glucose excursion could be the main target of anti-diabetic therapy for preventing the rise and worsening of cardio-vascular disease.

Repaglinide, a carbamoylmethilbenzoil derivated acid, has recently been introduced for controlling post-prandial hyperglycemia since it binds on beta-cell plasma membrane closing voltage-sensitive potassium channels, thereby activating the Ca ++ channels with increase in intracellular Ca++ influx [3]. Such latter event is responsible for an increase in intracellular calcium which in turn causes a burst in plasma insulin release[4,5].

Due to the fact that post-prandial glucose excursion is a strong cardio-vascular risk factoring diabetics[6,7,8,9], one cannot rule out that Repaglinide has also an impact on metabolic and coagulative factors related to cardio-vascular risk.

Metformin is a well known biguanides member, its blood sugar lowering effect does not depend on the presence of functioning beta-cell and its post-prandial blood sugar reduction is the main target of its mechanism of action[10].

Many studies are conducted to evaluate the effects of both Repaglinide and Metformin on post-prandial glucose excursion. Goldberg et al 1998 concluded that Repaglinide is safe and efficacious in lowering blood glucose and has potent glucose-lowering effect in the post-prandial hyperglycemia[11].

Davies MJ 2002 showed that Repaglinide, as compared with Metformin, it may be the ideal agent to be used very early in the disease process, or even in patients with impaired glucose tolerance, in whom early-phase insulin response is already lost[12].

**Patients and Methods:**
This study was conducted in Al-Hakeem diabetes center in Al-Saadr teaching hospital, Al-Najaf Al-ashraf governorate. Patients with type II DM were randomly divided into 2 groups : 1st group were already taking Repaglinide 1 mg twice daily 10 minutes before meal, the 2nd group were already taking Metformin 500 mg twice daily immediately after meal. Each group consist of 25 patients, the 1st group [16♂ and 9♀], 2nd group [5♂ and 20♀]. 2 hours post-breakfast blood sugar measurement was done for each patient by the convential glucose oxidase laboratory method. The data obtained were expressed as mean ± SEM with P-value was accepted at α= 0.05 and independent T-test was done to analyze the results obtained.

**Results:**
25 blood samples for each group were collected, post-prandial blood sugar was measured, the results were analyzed, the mean post-prandial blood sugar in patients taking Repaglinide was [172.22 mg/dl] ± SEM[1.22] and the range was 127-170 mg/dl,
while in patients taking Metformin was [169.28 mg/dl]± SEM [1.63] and the range was 153-186 mg/dl, independent T- test was implicated which appeared no significant difference between Repaglinide and Metformin in regard to their effects on post-prandial hyperglycemia [p > 0.05].

<table>
<thead>
<tr>
<th>Patients group</th>
<th>Mean 2 hr post-prandial blood sugar [mg/dl]±SEM</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repaglinide treated</td>
<td>172.22 ± 1.22</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Metformin treated</td>
<td>169.28 ± 1.63</td>
<td></td>
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</tbody>
</table>

Discussion:
Different studies were achieved to compare between different classes of anti-diabetic agents and between agents of the same group. Furlong et al 2002 found that Metformin combined with bedtime NPH insulin provides superior glycemic control to Repaglinide with less weight gain and improve diabetes treatment satisfaction[13].
Horton et al 2000 showed that Nateglinide Metformin monotherapy each improve overall glycemic control by different mechanism, Nateglinide decrease mealtime glucose excursion whereas Metformin primarily affect fasting blood sugar. In combination, Nateglinide and Metformin had complementary improving HbA1c, FBS and post—prandial-hyperglycemia[14].
Moses et al 1999 revealed that combined Metformin and Repaglinide therapy resulted in a superior glycemic control compared with Repaglinide or Metformin alone in patients with type II diabetes whose glycemia had not been well controlled on Metformin alone[15].
In this study, there is an agreement with Lund et al 2008 and Tarnow et al 2007 which resulted in the effect of Repaglinide on post-prandial hyperglycemia is comparable to that caused by Metformin, but Metformin achieved better cardio-vascular profile than Repaglinide[16,17].
My study results may also attributed to small sized samples and poor patients compliance and adherence to treatment regimen.

Conclusion and recommendation:
1- According to my study, Repaglinide has the same effect on post-prandial hyperglycemia as Metformin.
2- Further studies to evaluate the effects of both drugs on cardio-vascular profile and cost effectiveness are required.

References:


