Effect of intensive blood-glucose with metformin on complications in overweight patients with type 2 diabetes

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Study Type: POEM

Study Duration: mean follow-up = 10.7 yrs

Purpose: To compare conventional treatment (diet) with intensive treatment with metformin and then comparing these with those taking insulin or oral sulphonylureas.

Patients: 4209 patients of which 1704 patients overweight with glucose between 110 to 270; ~53 yrs; 54% female; 86% white; 8% black; ~86 kg; BMI = 31; BP = 140/86; small percentage on other therapy

Trial Design: Double-blinded, placebo-controlled, randomized, intention-to-treat, diet run-in, multicenter (15 UK centers), metformin (20%) versus diet alone (24%) versus those assigned to chlorpropamide (16%), glibenclamide (16%) and insulin (24%). Patients used diet for 3 months, then were allocated to different drug regimens depending on their blood sugar (>270). Clinical objective was to keep sugar as near 110 as possible.

Inclusion: newly diagnosed type 2 patients, aged 25-65

Exclusion: not mentioned

Outcome Events: Primary endpoint: any diabetes-related clinical endpoint, diabetes-related death, all-cause mortality

Secondary endpoints: MI, stroke, amputation, death due to PVD, microvascular complications

1. Are the results valid?

* randomized? yes
* double-blinded? yes
* placebo run in? no, but diet run-in
* were groups similar? yes
* all patients accounted for? yes

2. What were the results?

<table>
<thead>
<tr>
<th>Primary endpoint</th>
<th>Diet</th>
<th>metformin</th>
<th>RRR</th>
<th>ARR</th>
<th>P value</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any diabetes endpoint</td>
<td>39%</td>
<td>28.7%</td>
<td>32%</td>
<td>10.3%</td>
<td>.0034</td>
<td>10</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>21.7%</td>
<td>14.6%</td>
<td>36%</td>
<td>7.1%</td>
<td>.021</td>
<td>14</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.6%</td>
<td>3.5%</td>
<td>41%</td>
<td>2.1%</td>
<td>.032</td>
<td>48</td>
</tr>
</tbody>
</table>

NOT significant - diabetes-related death; MI; PVD death; microvascular complications

* single endpoint data - fatal MI favored the use of metformin, but others were not significantly different (i.e., non-fatal MI, sudden death, HF, angina, fatal and nonfatal stroke, death from PVD, death from renal disease, renal failure, etc)
* there was NO difference in any primary endpoint when diet alone was compared to insulin, chlorpropamide, or glibenclamide
* INTERESTING: when metformin is added to a sulphonylurea, there was an increase risk for diabetic-related deaths and all-cause mortality (p = NS), BUT, when data is combined to include metformin + any other treatment, the ARR is 6.3%, NNT = 16 (p = .03)

3. Will the results help me?

* those on insulin had the most hypoglycemic events
* those on metformin had the least hypoglycemic events
* there were no deaths due to lactic acidosis
* The median HbA1c was 7.4% in the metformin treated group, verses 8% in the diet-alone treated group
* metformin did not induce weight gain