The effects of metformin versus glibenclamide on complete blood picture in type 2 diabetic patients

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Abstract :
To assess the effects of metformin and glibenclamide each one alone on complete blood picture (CBP) in type 2 diabetic patients. A case control study. This study was conducted during the period from 1/5/2011 to 31/1/2012 in Ibn Sina hospital in Mosul city. CBP were measured in patients suffering from type 2 diabetes mellitus. Group 1: 21 patients on metformin therapy (850-1500mg/day), group 2: 23 patients on glibenclamide therapy (5-10mg/day), also 22 apparently healthy volunteers were taken as the control group. Blood samples were taken from the three groups and analyzed for full blood count including red blood cells count (RBCs) , white blood cell count (WBCs), and platelet count, hemoglobin (Hb) , mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and hematocrit (PCV). WBC count was higher in group 2 than that in group 1 and control group. The other parameters of complete blood picture in group 1 and 2 showed no significant differences compared with the control group. Metformin and glibenclamide have no significant effect on CBP except for the effect metformin which decreases WBC and platelet level which are already elevated in type 2 DM , but remain within the normal range. Such effect could not be seen in glibenclamide group.
Introduction
Diabetes mellitus (DM) is a group of metabolic disorders which consider carbohydrate metabolism and especially glucose is underutilized, producing hyperglycemia resulting from a defect in insulin secretion, insulin action, or both (1, 2). Type 2 diabetes, arises as a result of β cell failure combined with concomitant insulin resistance (3). Glibenclamide is a second generation sulfonylurea used in the treatment of type 2 diabetes (4). Sulphonylureas stimulate insulin secretion by interacting with specific receptors on the β cells surface (5). The frequency of adverse effects of glibenclamide is low, and the other effects are usually mild and reversible on withdrawal of the drug. The most common adverse effect is hypoglycemia (5), this may be profound and long lasting occasionally leading to permanent neurological damage or death (6). Other rare adverse effects are hematological (a granulocytes and hemolytic anemia) (7) and weight gain (5).

Metformin is a biguanide, which represents one of the oldest oral hypoglycemic agents used in the management of type 2 diabetes mellitus (8). The blood glucose-lowering actions of metformin result primarily from an amelioration of insulin resistance, mainly in liver and muscle, with a lesser effect in adipose tissue (9). Modest reductions in body weight often observed with metformin are associated with redistribution of fat from visceral depots to subcutaneous depots, which carry lesser cardiovascular (CV) risk (10, 11, 12, 13). Metformin is considered one of the safest oral hypoglycemic agents. It reduces insulin resistance but does not promote insulin secretion from β cells, and thus it is not associated with increased risk of hypoglycemia (13, 14). Minor untoward effect of metformin is lowering the levels of vitamin B12 and folate due to impaired gastrointestinal absorption and this effect has been documented with long term metformin therapy, but clinically these effects are insignificant and do not cause anemia (15). The effects of metformin and glibenclamide on complete blood picture (CBP) are not fully studied in human. Diabetes is a chronic illness that requires continuing medical care and patient self-management education to prevent acute and to reduce the risk of long-term complications (16). The most common agents used for the treatment of DM are metformin and glibenclamide therefore, this study was done to see whether these drugs affects CBP or not.

Materials and methods
This study was conducted from 1/5/2011 to 31/1/2012 in Al-Wafa Clinic for Treatment and Researches of Diabetes Mellitus in Ibn Sina Hospital in Mosul City. Forty four patients enrolled in this study were divided into two groups. The first group involved 21 type 2 diabetic patients (9 males and 12 females), their ages ranged between (52±5.55 and 44.8±10.7) respectively on regular treatment with metformin in doses ranged between 850-1500mg/day. The second group involved 23 type 2 diabetic patients (15 males and 8 females), their ages ranged between (51.8±5.09 and 52.2±7.7) respectively on regular treatment with glibenclamide in doses ranged between 5-10 mg/day. The control group included 22 apparently healthy volunteers, who had no chronic disease and did not received
any chronic medications. It consist of (13 males and 9 females), their ages ranged between (45.5±7.5 and 48.89±6.6) respectively. The study design was case – control study and patients were excluded if they had a history of any other diseases or those taking anti-diabetic drugs other than glibenclamide or metformin. Three milliliters of blood samples were collected from each individual (patients and controls) and all blood sample were transferred to EDTA tubes. The hematological parameters were measured by hematology auto analyzer (HORIBA ABX Coulter Counter , France, 9070T87726). Complete blood pictures parameters measured in this study included: red blood cells count (RBCs) ,white blood cell count (WBCs), Platelet count, hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and hematocrit (PCV). Data are presented as mean±SD. and paired t test was used for comparing the means of these groups (17). The level of significance was at p<0.05.

Results

The ages of the three groups (control group, metformin group and glibenclamide group ) is shown in table 1. No significant differences was found between the three groups. Tables 2 shows a comparison between complete blood picture parameter of control group, metformin group and glibenclamide group.

Table (1):- The ages of the studied groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control group N=22</th>
<th>Metformin group N=21</th>
<th>Glibenclamide group N=23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>47.5±7.1</td>
<td>46.52±4.14</td>
<td>51.52±6.65</td>
</tr>
</tbody>
</table>

Table (2):- Complete blood picture of control group metformin group and glibenclamide group.

<table>
<thead>
<tr>
<th>Hematological parameter</th>
<th>Control group N=25</th>
<th>Metformin group N=21</th>
<th>Glibenclamide group N=23</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBCs ($10^{12}$/L)</td>
<td>5.21±0.69</td>
<td>4.79±0.63</td>
<td>4.93±0.51</td>
</tr>
<tr>
<td>WBCs ($10^9$/L)</td>
<td>7.15±1.21</td>
<td>7.56±1.6</td>
<td>9.17±3.13*</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>14.44±2.12</td>
<td>14.05±2.34</td>
<td>14.53±1.7</td>
</tr>
<tr>
<td>Platelet ($10^9$/L)</td>
<td>234.1±58.8</td>
<td>232.4±59.4</td>
<td>254.5±84.5*</td>
</tr>
</tbody>
</table>
Discussion
Some studies on animals showed increased platelet aggregation and increased fibrinogen levels in diabetes (18). Diabetes also affects the erythrocytes causing an increase in the MCV (19). These increases were prevented by metformin in treatment (20). The age distribution in the three tested groups was chosen to be similar in order to exclude any effect that may affect on the CBP parameters (table 1). In this study, the results showed that there were no significant differences in all CBP parameters (except WBC and platelet) in the three tested groups (table 2), this is in agreement with other similar studies (21, 22, 23). The results also showed that there was a significant increase in WBC in glibenclamide group with no such effect in metformin group as compared with control (table 2), this may be due to DM which may increase WBC and metformin decreases these elevations but glibenclamide has no such effect (20). Also elevated WBC count, even within the normal range, is associated with both macro- and microvascular complications in type 2 diabetes (24, 25, 26). Arnon (27) showed that there was decreased WBC after metformin treatment which returned to the normal range after discontinuation of metformin therapy. However the inter-individual variation and environment are contributing factors (28). In addition, changes in environmental temperatures were associated with changes in WBC count (29, 30). Platelet level showed no changes in metformin group, but little elevation could be seen in glibenclamide group as compared with control group but still within the normal ranges (table 2). Again this effect could be due to the metformin ability to decrease the platelet count. This is in agreement with many studies (31, 32) observed that the level of platelet was decreased after metformin treatment. This effect may be due to other antithrombotic mechanisms of metformin include stabilization of reduced aggregation of platelet.

Conclusion
In conclusion, metformin and glibenclamide have no significant effect on CBP except metformin which decreases WBC and platelet levels. These are already increased in type 2 DM, but remain within the normal range. Such effect could not be seen with glibenclamide. The periodical examination of metformin and glibenclamide type 2 diabetic treated patients for CBP is necessary because elevation in some parameters are associated with complication of disease.
References


