Utilization of Chronic Medications with Metabolic Effects and Risk for Incident Diabetes in Postmenopausal Women


BACKGROUND
Recent studies suggest that thiazide diuretics (TD), statins (ST), β-adrenergic blockers (BB), antidepressants (AD) and atypical antipsychotics (AP) can impair glucose homeostasis and increase risk for diabetes. It is unclear to what degree these agents might be used simultaneously and whether and to what extent simultaneous use will increase the long-term risk for diabetes. Because many of these medications are used to prevent CV morbidity and are often prescribed in combination for many years, exploration of additive or exponential effects on diabetes manifestation is critical.

OBJECTIVE
The objective of this analysis is to investigate 1) the patterns of use of medications that may influence glucose homeostasis among nondiabetic women enrolled in the Women’s Health Initiative (WHI) and 2) the association between these medication use patterns and incidence of diabetes within the WHI.

METHODS
In the 161,808 participants enrolled in the observational study (OS) and the clinical trial (CT) WHI cohorts, we conducted an analysis of self-reported use of medications within five drug classes: TD, ST, BB, AD and AP. We categorized patients according to those taking one, two, or three drugs from these classes at baseline and at the three year visit. Lastly we investigated the distribution of incident diabetes during an average of 7.6 years of follow-up, according to self-reported use of one or more medications from these five drug classes at baseline. Diabetes was determined by self-report of ever having received a physician diagnosis of and/or treatment for diabetes when not pregnant. Diabetes status was recorded at baseline and annually. Women with diabetes at baseline were excluded from this analysis.

RESULTS
A total of 152,080 women without diabetes at baseline and with data regarding self-reported use of medications were included in this analysis. There were a total of 12,049 cases of incident diabetes identified over more than 1 million person-years of follow-up. Frequency of use of a single or multiple drugs from the five drug classes at baseline and year 3 as well as frequency of incident diabetes by medication use is summarized in the Table. Overall, single use of a drug from one of the five classes was most common, and drug use (single or combination) increased from baseline to year 3. Compared with unadjusted incidence in women not taking any medications from the 5 drug classes (7.5%), the unadjusted incidence of diabetes was significantly greater as use of medications from the 5 drug classes increased (p<0.0001), Table.

<table>
<thead>
<tr>
<th></th>
<th>Single Drug Use (patients in thousands)</th>
<th>Top 3 Two Drug Combinations (patients in thousands)</th>
<th>Top 3 Three Drug Combinations (patients in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TD</td>
<td>ST</td>
<td>BB</td>
</tr>
<tr>
<td>Baseline</td>
<td>16.0</td>
<td>10.8</td>
<td>12.2</td>
</tr>
<tr>
<td>3 Year</td>
<td>17.5</td>
<td>18.5</td>
<td>15.7</td>
</tr>
<tr>
<td>Overall Incidence of Diabetes</td>
<td>11.02% in women taking any single medication</td>
<td>14.7% in women taking any two drug combination</td>
<td>18.5% in women taking any three drug combination</td>
</tr>
</tbody>
</table>

CONCLUSION
At both the baseline and 3 year visit women took a single drug from the specified drug classes most frequently, however use of 2 and 3 drug combinations did increase over time. The unadjusted incidence of diabetes was higher in women taking multiple medications from classes of drugs known to be associated with adverse metabolic effects. Future efforts will include identifying how much of this increase in incidence can be attributed to possible population differences between women taking a single medication from one of these classes versus those taking more than one medication. However, the increased use coupled with the increased risk for incident diabetes suggest strategies to identify women at risk for the metabolic side effects of these drugs are warranted and ongoing monitoring for diabetes risk is justified when medications from these classes are prescribed.

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